ethanol gave 9-chloro-5-methylamino-2-phenyl-4H-1,3,6-benzoxadiazocine (11) as beige needles: mp 240–243° dec with sintering at 180°; ir 3460, 1660, 1620, 1480 cm^{-1}; uv max 245 mμ (ε 23,000); mass spectrum *m/e* 299, 230, 196 (-C_6H_5CN), 167, 154; nmr (DMSO), δ 2.48 (d, 3, *J* = 5 Hz, -$NHCH_3$) and 4.03 (s, 2, -CH_2-) ppm.

Anal. Calcd for $C_{16}H_{14}ClN_3O$: C, 64.11; H, 4.71; N, 14.02. Found: C, 64.14; H, 4.79; N, 14.16.

To a solution of 5 g of the above mixture of 11 and 12a in 125 ml of hot ethanol was added 25 ml of 1 *N* hydrochloric acid, and the mixture was heated on the steam bath for 5 min. Dilution to 375 ml with water and cooling gave 2.8 g of crude 2-benzamido-4′-chloro-2′-hydroxyacetanilide (13a), mp 228–234° dec. Recrystallization from methanol gave grayish prisms: mp 233–236° dec; ir (KBr) 1665, 1540 cm^{-1}; uv max 290 mμ (ε 7400), 257 (sh) (14,200) and 248 (19,000); mass spectrum *m/e* 304, 286, 268, 162 ($C_6H_5CONH-CH_2C^+O$), 143, 134, 105.

Anal. Calcd for $C_{15}H_{13}ClN_2O_3$: C, 59.12; H, 4.30; N, 9.20. Found: C, 59.49; H, 4.31; N, 9.20.

The aqueous mother liquors left after separation of **13a** were neutralized with concentrated ammonium hydroxide, and 2.2 g of 4-benzoyl-6-chloro-3,4-dihydro-2-methylaminoquinoxaline (**12a**), mp 216–222° dec, precipitated. Recrystallization from ethanol gave colorless needles: mp 220–230° dec; ir (KBr) 3430, 1630, 1575 cm^{-1}; uv max 320 mμ (sh) (ε 5100), 290 (sh) (13,500) and 262 (21,000); mass spectrum *m/e* 299, 194, 165, 153.

Anal. Calcd for $C_{16}H_{14}ClN_3O$: C, 64.11; H, 4.71; N, 14.02. Found: C, 63.92; H, 4.97; N, 13.84.

Thin layer chromatography (10% MeOH-$CHCl_3$ on silica gel G) showed that 11 was converted into 13c while 12a remained unchanged.

2-Benzamido-2′-hydroxyacetanilide (13b).—A mixture of 1.2 g (4 mmol) of 2-benzamido-4′-chloro-2′-hydroxyacetanilide (**13a**), 8 g of Raney nickel slurry, 1 ml of triethylamine, and 200 ml of ethanol was hydrogenated at room temperature and atmospheric pressure until 105 ml of hydrogen was taken up. The catalyst was filtered, and the filtrate acidified with acetic acid. This solution was concentrated *in vacuo*, and water was added to the residue to give 1 g of **13b**, mp 199–203°. Recrystallization from ethanol gave 0.6 g, mp 202–204°, undepressed on admixture with a sample prepared from hippuryl chloride[8] and *o*-aminophenol. The infrared spectra were also identical.

1-Benzoyl-7-chloro-1,2-dihydro-3-(N-methylacetamido)quinoxaline (12b).—A mixture of 24 g (80 mmol) of **12a**, 1.6 g of sodium acetate, and 200 ml of acetic anhydride was warmed on a steam bath until a clear solution was obtained and then stirred without further heating for 1 hr. The residue left on removal of the acetic anhydride *in vacuo* was crystallized from ether and then recrystallized from benzene–hexane to give 23.6 g (84%) of **12b**: mp 123–126°; ir 1690, 1660, 1615 cm^{-1}.

Anal. Calcd for $C_{18}H_{16}ClN_3O_2$: C, 63.25; H, 4.71. Found: C, 63.26; H, 4.91.

4-Benzoyl-6-chloro-3,4-dihydroquinoxalin-2(1H)-one (14).[9]—A mixture of 8.54 g (25 mmol) of **12b**, 125 ml of dioxane, and 25 ml of 1 *N* hydrochloric acid was allowed to stand at room temperature for 2.5 hr, and then diluted with ice water to 500 ml. The precipitate was collected and washed with ether to give 5.4 g (80%) of **14**, mp 259–263°, identified by mixture melting point and infrared spectra.

Irradiation of 9 with Isolation of 10.—A solution of 2 g of **9** in 150 ml of ethanol was irradiated for 55 min through a Pyrex filter. The solution was concentrated *in vacuo* and the residue crystallized from ether to give 1.3 g of the crude oxaziridine **10** which was purified by filtration of a solution in ether–methylene chloride through 60 g of Florisil and elution with ether. The residue obtained on concentration of the filtrate (reduced pressure, 40°) was crystallized from ether to yield 0.9 g of **10** which showed on tlc (silica gel G–ethyl acetate) only a trace of **9**. A solution of 0.6 g of this material in 150 ml of ethanol was then irradiated as before and aliquots were removed at 5 min intervals. Examination of these aliquots by tlc in the above system showed that the trace of **9** disappeared in 10 min. This was followed by a gradual formation of **11** and **12a** until after 3 hr **11** and **12a** were the main components contaminated only by a trace of **10**.

Registry No.—**2a**, 17953-20-7; **2b**, 17953-21-8; **6**, 17953-22-9; **10**, 17953-23-0; **11**, 17953-24-1; **12a**, 17953-25-2; **12b**, 17953-26-3; **13a**, 17953-27-4; **13b**, 17953-28-5.

Acknowledgment.—We thank Mr. S. Traiman for the infrared spectra, Dr. T. Williams for the nmr spectra, Dr. V. Toome for the ultraviolet spectra, Dr. F. Vane for the mass spectra, Dr. F. Scheidl for the microanalyses, and Mr. T. Flynn for his skillful technical assistance.

Reaction of N,N-Dichlorourethan with Indole and Derivatives[1]

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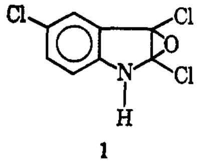
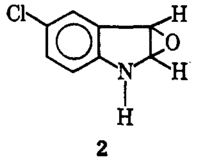
Received May 17, 1968

Contrary to literature reports, the major product of reaction of N,N-dichlorourethan (DCU) with indole and indole-2- or -3-carboxylic acid is 3,3,5-trichlorooxindole (5). Reaction of the methyl esters with DCU yields 2-carbomethoxy-2,5,7-trichloroindoxyl (8) and 3-carbomethoxy-3,5-dichlorooxindole (10), respectively. Structures have been assigned by physical and chemical methods.

The report of Chabrier[4] that reaction of N,N-dichlorourethan (DCU) with indole-2-carboxylic acid yields 2,3,5-trichloro-2,3-epoxyindole (1), a high melting, stable compound, aroused our interest. By neutral dehalogenation 1 might, hopefully, be converted into the corresponding oxirene, an unknown small-ring compound.



1



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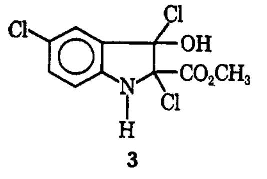

3

Aside from the apparent failure of 1 to undergo facile halogen migration, as 2-chloro epoxides are prone to do,[5] it was surprising that reduction was claimed to yield the dihydro product, 5-chloro-2,3-epoxyindoline

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[1] Pseudohalogens. XII. Part XI: H. C. Hamann and D. Swern, *J. Amer. Chem. Soc.*, **90**, 6481 (1968).

[2] Eastern Regional Research Laboratory, U. S. Department of Agriculture, Philadelphia, Pa. 19118.

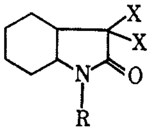
[3] To whom enquiries should be addressed. The authors acknowledge with thanks support of this investigation by U. S. Public Health Service Grants No. CA-07803 and CA-07174 from the National Cancer Institute.

[4] P. Chabrier, *Ann. Chim.*, **17**, 353 (1942).

[5] R. N. McDonald and P. A. Schwab, *J. Org. Chem.*, **29**, 2459 (1964); *J. Amer. Chem. Soc.*, **85**, 4004 (1963).

(2), cleanly and in high yield without destruction of the epoxide function. Furthermore, reaction of the methyl ester of indole-2-carboxylic acid with DCU under similar conditions was also reported to yield a product with three chlorine atoms, assigned the improbable structure 2,3,5-trichloro-2-carbomethoxy-3-hydroxyindoline (**3**), but only *one* chlorine atom could be removed by reduction to yield an unidentified product.

The reaction of positive halogen sources, such as the hypohalous acids, with N-alkylindoles has long been known to yield 3,3-dihalooxindoles (**4**).[6-8] The discrepancy between these results and those of Chabrier prompted us to reexamine the reactions of DCU with indole, indole-2- and -3-carboxylic acids, and their methyl esters.



4, R = alkyl; X = Cl, Br

Results and Discussion

Reaction of 2 mol of DCU (four atoms of positive chlorine) with 1 mol of indole (**5a**), indole-2-carboxylic acid (**5b**), or indole-3-carboxylic acid (**5c**) in 80:20 acetic acid–water at 25–35° gave 3,3,5-trichlorooxindole (**5**), mp 191–192°, as the major product (40% yield from indole; 85–90% from the carboxylic acids). Although the melting point of **5** (191–192°) agreed essentially with that reported by Chabrier (188°) and its elemental analysis was also consistent with the molecular formula of **1**, $C_8H_4Cl_3NO$, the ir spectrum showed strong carbonyl absorption, thus eliminating **1** as a possible structure. Absorption at 1760 (C=O), 3480 (NH), and 1630 cm^{-1} (aromatic) permitted a tentative structural assignment of **5** as a halo-substituted oxindole,[9] confirmed by chemical evidence. Reduction of **5** with zinc–copper couple in glacial acetic acid gave the known 5-chlorooxindole (**6**),[10] mp 195–196°, in 75% yield. Hydrolysis of **5** in refluxing aqueous methanol yielded 5-chloroisatin (**7**) (85% yield), which on reduction with zinc–copper couple in glacial acetic acid also gave **6** (65% yield).[11]

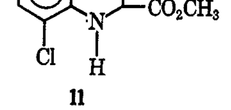
Reaction of 1 mol of methyl indole-2-carboxylate (**8a**) with 2 mol of DCU as described for the free acid gives 2-carbomethoxy-2,5,7-trichloroindoxyl (**8**), mp 203–204°, in almost 90% yield, not **3** as claimed.[4] The structure of **8** was determined by elemental analysis and spectral and chemical means. Besides ir absorption at 3450 (NH) and 1620 cm^{-1} (aromatic), two carbonyl bands were obtained at 1750 and 1720 cm^{-1} corresponding, respectively, to ester and ketone functionality. The nmr spectrum showed absorption at 7.52 (2 H, J = 3 cps), consistent with *meta* substitution of the chlorine atoms in the aromatic nucleus, 3.28 (1 H, N–H) and 3.88 ppm (TMS, 0) (3 H, OCH_3). Reduction of **8** with zinc–copper couple in glacial acetic acid removed only one chlorine atom and gave 5,7-dichloroindoxyl (**9**), mp 242–243°, in 80% yield. Its ir spectrum showed absorption at 3300 (NH), 1725 (C=O), and 1610 cm^{-1} (aromatic). The nmr spectrum (signal at 7.38 ppm, 2 H, J = 3 cps) indicated *meta* substitution of the chlorine atoms in the aromatic ring and, in addition, the nmr spectrum contained two weakly split singlets (2 H and 1 H, $J \leq 1$ cps) at 3.62 and 3.24 ppm, respectively. Treatment of **9** with deuterium oxide and a trace of trifluoroacetic acid caused the singlet at 3.24 (NH) to disappear and the methylene protons at 3.62 ppm to coalesce to a sharp singlet.

In contrast with the identical behavior of indole-2- and 3-carboxylic acids on reaction with DCU, methyl indole-3-carboxylate (**10a**) behaved differently from the 2 isomer and gave 3-carbomethoxy-3,5-dichlorooxindole (**10**), mp 195–196°, in about 75% yield. Its structure was confirmed by its ir spectrum and facile reduction to 5-chlorooxindole (**6**) in 89% yield.

The products of reaction of DCU with indole and its derivatives can be rationalized by a single assumption, namely, that DCU in aqueous acetic acid generates electropositive chlorine which is the reactive species.[12a] It is of interest that DCU in acetic acid is an excellent source of positive halogen, whereas in benzene DCU behaves as a free-radical source.[12b]

The reactions that have been described proceed extremely rapidly at about 30° and are complete usually within 30 min thus precluding the isolation of intermediates. With the exception of indole as starting material yields of products are high. Although we visualize that chlorination of the aromatic ring occurs as the last step in the chlorination process, it may be occurring concurrently. The exact time such chlorination occurs is not relevant to the major argument that Cl^+ is the sole active species required to rationalize the products obtained.

Reduction of **8** and **10** to **9** and **6**, respectively, by zinc–copper couple in acetic acid, should proceed *via* the dehalogenated species, **11** and **12**, respectively, which undergo acidolysis in refluxing acetic acid followed by facile decarboxylation, as expected of *β*-keto acids.



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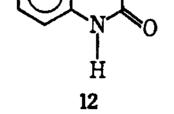

12

Experimental Section

N,N-Dichlorourethan (DCU) was prepared by chlorination of urethan in buffered aqueous solution.[12b] Indole and indole-2- and indole-3-carboxylic acids were obtained from Aldrich Chemical Co. and were used as received. Ir spectra were obtained on a Perkin-Elmer Infracord 137. Nmr spectra were obtained on a Varian A-60A spectrometer using tetramethylsilane as internal standard. Microanalyses were performed by Microanalysis, Inc., Wilmington, Del.

3,3,5-Trichlorooxindole (**5**). A.—Indole-2-carboxylic acid (**5b**) (3.22 g, 0.020 mol) was suspended in acetic acid–water (80:20) (60 ml) in a 100-ml three-neck flask equipped with a stirrer, thermometer, and dropping funnel. DCU (6.32 g, 0.040

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(6) E. Fischer and O. Hess, *Ber.*, **17**, 564 (1884).

(7) H. G. Coleman, *Ann.*, **248**, 116 (1888).

(8) A. Michaelis, *Ber.*, **30**, 2811 (1897).

(9) A. E. Kellie, D. G. O'Sullivan, and P. W. Sadler, *J. Chem. Soc.*, 3809 (1956).

(10) W. B. Wright, Jr., and K. H. Collins, *J. Amer. Chem. Soc.*, **78**, 221 (1956). The melting point given by Chabrier for the reduction product of **1** was 192°.

(11) W. C. Sumpter, *Chem. Rev.*, **34**, 393 (1944).

(12) (a) J. C. Powers, *J. Org. Chem.*, **31**, 2627 (1966); (b) T. A. Foglia and D. Swern, *ibid.*, **31**, 3625 (1966).

mol) was added dropwise to the stirred suspension maintained at 30–35° by an ice–water bath. The mixture became homogeneous when DCU addition was complete, and it was stirred for an additional 0.5 hr. The reaction solution was poured into water (300 ml), and the precipitate of **5** was filtered and dried (4.32 g, 92% yield): mp 186–190° (lit.[4] mp 188°).

Analytically pure **5**, mp 191–192°, was obtained by recrystallization from benzene: ir ($CHCl_3$) 3480 (NH), 1760 (C=O), 1630 (C=C), 1480, 1190, 1180, 970, 850, 825 cm^{-1}.

Anal. Calcd for $C_8H_4Cl_3NO$: C, 40.63; H, 1.70; Cl, 44.97; N, 5.92. Found: C, 40.49; H, 1.66; Cl, 45.10; N, 5.71.

B.—Indole-3-carboxylic acid (**5c**) (3.22 g, 0.020 mol) was treated with DCU as just described to give **5** (4.20 g, 89% yield), mp 180–185°, identical in every respect (melting point, mixture melting point, ir, nmr) with that obtained from the 2 isomer.

C.—Indole (**5a**) (2.34 g, 0.020 mol) yielded crude **5** (4.20 g), mp 150°, containing considerable colored tarry material. Recrystallization failed to yield the pure product. Chromatography on Florisil (1 g of crude **5**/40 g of adsorbent) and elution with 75% ether–pentane yielded analytically pure **5**, mp 188–191° (0.4 g, 40%), identical in every respect with that obtained from **5b** and **c**.

5-Chlorooxindole (**6**).—To a stirred solution of **5** (2.36 g, 0.01 mol) in hot glacial acetic acid (20 ml), zinc–copper couple[13] (7.0 g in 25 ml of acetic acid) was added, and the mixture was refluxed for 18 hr. After filtration, the filtrate was poured into water (250 ml) and the precipitated solid was filtered and dried: yield of crude **6**, 1.32 g (75%); mp 190–195°. Analytically pure **6**, mp 198–198.5° (lit. mp 192° [4] and 195–196° [10]), was obtained by two recrystallizations from ethanol: ir ($CHCl_3$) 3480 (N–H), 1740 and 1710 (C=O), 1640 (C=C), 1480, 1160, 1100, 870 cm^{-1}.

Anal. Calcd for C_8H_6ClNO: C, 57.33; H, 3.61; Cl, 21.15; N, 8.36. Found: C, 57.23; H, 3.73; Cl, 21.03; N, 8.31.

5-Chloroisatin (**7**).—A solution of **5** (1.18 g, 0.005 mol) in 50% aqueous methanol (50 ml) was refluxed for 6 hr, and the cooled solution was poured into water (250 ml). The precipitated red solid was filtered and dried: yield of crude **7**, 0.80 g (85%); mp 250–252°. Analytically pure **7**, mp 251–252° (lit.[14] mp 246–247°), was obtained by two recrystallizations from ethanol: ir ($CHCl_3$) 3460 (N–H), 1760 (C=O), 1620 (C=C), 1470, 1445, 1290, 1190, 1170, 965, 845 cm^{-1}.

Anal. Calcd for $C_8H_4ClNO_2$: C, 52.92; H, 2.22; Cl, 19.52; N, 7.71. Found: C, 52.46; H, 2.40; Cl, 19.60; N, 7.67.

Reduction of **7** (1.40 g, 0.008 mol) with zinc–copper couple as described for **5** also yielded **6**, mp 194–196° (0.85 g, 65%), identical in every respect (ir, melting point, mixture melting point) with an authentic sample.

Methyl Indole-2-carboxylate (**8a**).—This was prepared in 90% yield from **5b** by conventional esterification with methanol (sulfuric acid catalyst), mp 151–152° (lit.[15] mp 150–151.5°).

Methyl Indole-3-carboxylate (**10a**).—As described for the 2 isomer **5c** was converted into analytially pure **10a** in 60% yield: mp 146–147° (lit.[16] mp 147–148°).

2-Carbomethoxy-2,5,7-trichloroindoxyl (**8**).—**8a** (3.50 g, 0.020 mol) was treated with DCU as previously described for **5a–c** to give crude **8** (4.3 g, 90% yield), mp 191–195° (lit.[4] mp 184°). Analytically pure **8**, mp 203–204°, was obtained after two crystallizations from ethanol: ir ($CHCl_3$) 3450 (N–H), 1750 and 1720 (C=O), 1620 (C=C), 1470, 1220, 1170, 1040, 875 cm^{-1}.

Anal. Calcd for $C_{10}H_6Cl_3NO_3$: C, 40.78; H, 2.05; Cl, 36.11; N, 4.76. Found: C, 40.53; H, 2.35; Cl, 36.03; N, 5.07.

5,7-Dichloroindoxyl (**9**).—A solution of **8** (1.50 g, 0.005 mol) was reduced with zinc–copper couple (3.25 g) in acetic acid (35 ml) as described for the reduction of **5** to give **9** (0.8 g, 80% yield), mp 241–242°. Analytically pure **9**, mp 242–243°, was obtained by recrystallization from ethanol: ir (Nujol) 3300 (N–H), 1725 (C=O), 1610 (C=C), 1450, 1305, 1215, 1170, 945, 875, 860, 715 cm^{-1}.

Anal. Calcd for $C_8H_5Cl_2NO$: C, 47.56; H, 2.50; Cl, 35.09; N, 6.93. Found: C, 47.79; H, 2.54; Cl, 34.81; N, 6.74.

3-Carbomethoxy-3,5-dichlorooxindole (**10**).—**10a** (3.50 g, 0.02 mol) was treated with DCU as previously described for **5a–c** and **8a** to give **10** (3.70 g, 75% yield), mp 192–195°. Recrystallization from ethanol yielded pure **10**: mp 195–196°; ir ($CHCl_3$) 3400 (N–H), 1760 and 1740 (C=O), 1620 (C=C), 1470, 1445, 1290, 1190, 1170, 855 cm^{-1}.

Anal. Calcd for $C_{10}H_7Cl_2NO_3$: C, 46.18; H, 2.71; Cl, 27.26; N, 5.39. Found: C, 46.44; H, 2.78; Cl, 27.02; N, 5.27.

Reduction of **10** (1.30, 0.005 mol) with zinc–copper couple (3.25 g) in hot acetic acid gave 5-chloroxindole (**6** 0.75 g, 89% yield), mp 191–193°, identical with an authentic sample (melting point, mixture melting point, ir).

Registry No.—N,N-Dichlorourethan, 13698-16-3; **5**, 17630-74-9; **5a**, 120-72-9; **6**, 17630-75-0; **7**, 17630-76-1; **8**, 17630-77-2; **9**, 17630-79-4; **10**, 17630-78-3.

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(13) E. LeGoff, *J. Org. Chem.*, **29**, 2048 (1964).

(14) N. Buu-Hoi, *Rec. Trav. Chim. Pays Bas*, **73**, 197 (1954).

(15) C. Zatti and J. Ciaician, *Ber.*, **21**, 1929 (1888).

(16) C. Zatti and A. Ferratini, *ibid.*, **23**, 2296 (1890).

Reaction of Tosyl Isocyanate with Carboxylate Salts[1]

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p-Toluenesulfonyl isocyanate reacts readily with carboxylate salts at room temperature to give N-acyl-*p*-toluenesulfonamides. Benzenediazonium-2-carboxylate, however, gives a more complex reaction leading ultimately to N-(*o*-azidobenzoyl)-*p*-toluenesulfonamide. The mechanism of this reaction is discussed.

The reaction of benzyne with phenyl isocyanate was studied by Sheehan and Daves,[2] who found only products derived from 1,4 addition, phenanthridone and 6-phenoxyphenanthridine. In view of the tendency of isocyanates (and other cumulated double-bond systems) to give 1,2 cycloadditions in some cases[3] we felt that investigation of the reaction of benzyne with isocyanates incapable of reacting by 1,4 addition would be of interest as a route to benzazetinones[4] *via* 1,2 cycloaddition.

This led us to decompose benzenediazonium-2-carboxylate (I) in solutions of aliphatic isocyanates and of tosyl isocyanate (II) in the hope of obtaining benzazetinone products *via* 1,2 cycloaddition. Although no such 1,2 cycloadditions were found, a reaction of tosyl isocyanate with I and with other carboxylate salts was found. This reaction constitutes the major portion of this paper.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Infracord, Model 137-B, calibrated with a polystyrene film. Proton magnetic resonance spectra were obtained on a Varian A-60 spectrometer and are reported as τ values relative to tetramethylsilane as internal standard (τ 10.00). All melting points are un-

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(1) Presented in part before the Division of Organic Chemistry, 154th Meeting of the American Chemical Society, Chicago, Ill, Sept 13, 1967.

(2) J. C. Sheehan and G. D. Daves, Jr., *J. Org. Chem.*, **30**, 3247 (1965).

(3) H. Ulrich, "Cycloaddition Reactions of Heterocumulenes," Academic Press, New York, N. Y., 1967, pp 135–189.

(4) E. M. Burgess and G. Milne, *Tetrahedron Lett.*, 93 (1966).