17631-20-8; **4f**, 17631-21-9; **4g**, 17631-22-0; **4h**, 17631-23-1; **4i**, 17631-24-2; **8**, 1530-47-8; **10** (R = *p*-BrC_6H_4; R′ = R″ = H), 17631-26-4; **11**, 2689-60-3.

Acknowledgment.—We are indebted to Dr. A. Selva for the mass spectra. We wish to thank Mr. A. Arnone for his assistance in taking the nmr spectra.

Quinazolines and 1,4-Benzodiazepines. XLII.[1] Photochemistry of Some N-Oxides

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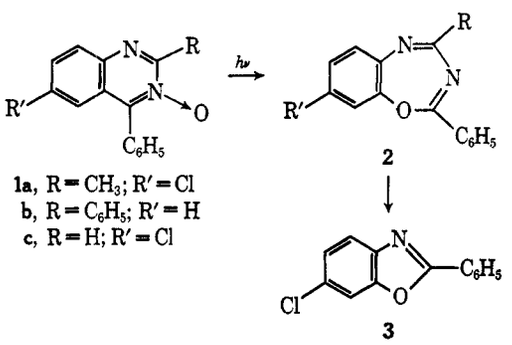
Quinazoline 3-oxides **1** are photoisomerized to benzo[*f*]-1,3,5-oxadiazepines **2**. 6-Chloro-2-methyl-4-phenylquinazoline 1-oxide (**4**) gives 1-acetyl-5-chloro-3-phenylindazole (**6**) on irradiation. 7-Chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 3-oxide (**9**) gives a mixture of 9-chloro-5-methylamino-2-phenyl-4H-benzo[*g*]-1,3,6-oxadiazocine (**11**) and 1-benzoyl-7-chloro-1,2-dihydro-3-methylaminoquinoxaline (**12a**). These transformations are believed to proceed by rearrangement of the oxaziridines formed as primary isomerization products.

Aromatic N-oxides are quite generally labile to irradiation with ultraviolet light,[2] as illustrated by the photoisomerization of quinazoline 3-oxides **1** to benzo-[*f*]-1,3,5-oxadiazepines **2**.[3] We wish to report two further examples of this isomerization as well as the photochemical behavior of two related N-oxides.



1a, R = CH_3; R′ = Cl
b, R = C_6H_5; R′ = H
c, R = H; R′ = Cl

2

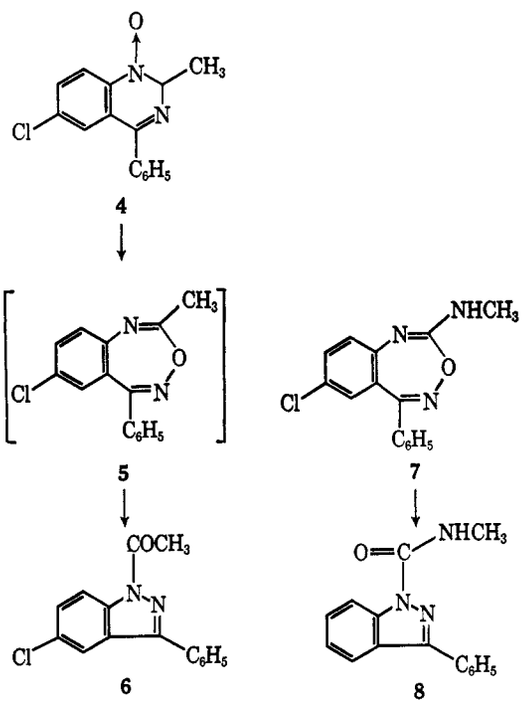
3

The irradiation products **2a** and **2b** were obtained in excellent yield; however, irradiation of **1c** gave only a low yield of **3**. Presumably **3** was formed from **2c** during work-up of the reaction mixture.[4]

In an attempt to obtain evidence for the presence of isolable intermediates in the photoisomerization of **1a**, the ultraviolet spectrum of an irradiated acetonitrile solution of **1a** was measured at intervals. These spectra showed isosbestic points at 298, 332, and 345 mμ which would indicate the absence of stable intermediates.

The quinazoline 1-oxide **4**[5] was also irradiated. By analogy with the quinazoline N-oxides the formation of **5** was expected.[2c] The product, however, displayed a prominent carbonyl band at 1720 cm^{-1} and was readily identified as **6** by comparison with a sample obtained by acetylation of 5-chloro-3-phenylindazole. Its formation *via* **5** as an intermediate is not ruled out since it has been shown that **7**, synthesized by non-photochemical means, gave **8** on exposure to light (Scheme I).[6]

SCHEME I



4

5

6

7

8

The photochemistry of the benzodiazepine 4-oxide **9**, which may be considered to be a homoquinazoline N-oxide, was reinvestigated. It has been reported that irradiation with sunlight gives the oxaziridine **10**[7] which is reconverted into **9** on heating (Scheme II). Irradiation of **10**, formed as primary product,[7] or more vigorous irradiation of **9** led to the formation of two new photoisomers **11** and **12a**. Direct crystallization of the reaction mixture gave **11** which was shown to be isomeric with the starting material by elemental analysis and mass spectrometry. Mild acid hydrolysis of **11** gave **13a** whose structure was proved by dechlorination to **13b**.[8] In addition, structure **11** was supported

(1) Paper XLI: A. Stempel, I. Douvan, and L. H. Sternbach, *J. Org. Chem.*, **33**, 2963 (1968).

(2) (a) O. Buchardt, B. Jensen, and I. K. Larsen, *Acta. Chem. Scand.*, **21**, 1841 (1967); (b) O. Buchardt and J. Fenney, *ibid.*, **21**, 1399 (1967); (c) C. Kaneko, S. Yamada, I. Yokoe, and M. Ishikawa, *Tetrahedron Lett.*, 1873 (1967); (d) O. Buchardt, *ibid.*, 6221 (1966); (e) O. Buchardt, C. Lohse, A. M. Duffield, and C. Djerassi, *ibid.*, 2741 (1967).

(3) C. Kaneko and S. Yamada, *ibid.*, 5233 (1967).

(4) See ref 2 for a similar ring contraction.

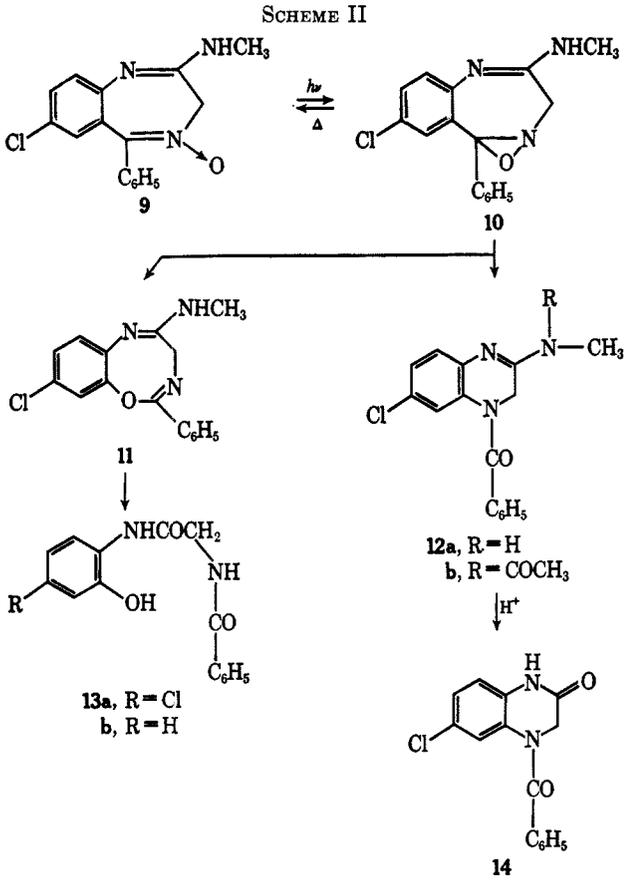
(5) L. H. Sternbach, S. Kaiser, and E. Reeder, *J. Amer. Chem. Soc.*, **82**, 475 (1960).

(6) W. Metlesics, G. Silverman, and L. H. Sternbach, *Monatsh. Chem.*, **98**, 633 (1967).

(7) L. H. Sternbach, B. A. Koechlin, and E. Reeder, *J. Org. Chem.*, **27**, 4671 (1962).

(8) J. L. Abernathy and G. L. Leonardo, *J. Chem. Educ.*, **41**, 53 (1964).

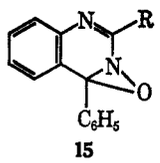
SCHEME II



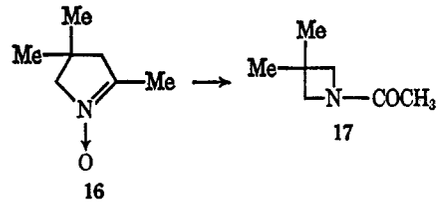
by the infrared spectrum which shows a band at 3460 cm^{-1} (consistent with an NH group but not with an OH group) and the nmr spectrum which shows a doublet at δ 2.84 (3, J = 5 Hz, $-NHCH_3$) and a singlet at 4.03 (2, $-CH_2-$).

The other photoisomerization product **12a** was isolated after mild acid hydrolysis of the whole reaction mixture. This converted **11** into **13a** which was insoluble in acid while **12a** remained in solution. The structure of **12a** was proved by acetylation to **12b** which, on mild acid hydrolysis, gave the known **14**.[9]

It has been postulated that the isomerization of quinazoline 3-oxides **1** to benzoxadiazepines **2** proceeds by way of the unisolated[2] oxaziridines **15**. Isolation of the oxaziridine **10**[7] and its photoisomerization thus support the above postulate, although **15** was not isolated owing to its apparent instability. Since **10** reverts to **9** on heating without giving **11** or **12a**, analogy suggests that the ring expansion of **15** to the benzoxadiazepines **2** is a photochemical process.



The stability of the oxaziridine **10** permits an additional possible type of photoisomerization to **12a**. This second path is analogous to the transformation of the aliphatic nitrone **16** into **17**.[10] Furthermore,



participation of the 1,2 double bond in the ring expansion of **15** to **2** is indicated since where its proximity to the nitrone function is decreased by insertion of a methylene group as in **9** a second type of product **12a** appears.

Experimental Section[11]

Irradiation of Quinazolines.—A solution of 10 g of the quinazoline **1** in 1.4 l. of benzene was irradiated with a Hanovia 200-W medium-pressure lamp in a quartz immersion well until thin layer chromatography indicated the disappearance of starting material. Times were 16–96 hr. The solution was then concentrated *in vacuo*.

6-Chloro-2-phenylbenzoxazole (3).—Crystallization of the residue from irradiation of **1c** from methanol gave 2.5 g of crude **3**. Three recrystallizations from ethanol gave a pure sample, mp 106–108° (lit.[12] mp 98–100°), undepressed on admixture of authentic material.

8-Chloro-4-methyl-2-phenyl-1,3,5-benzoxadiazepine (2a).—Crystallization of the residue from irradiation of **1a** from ether gave 8.3 g of **2a**, mp 133–138°. Recrystallization from ethanol gave yellow needles: mp 137–140°; ir 1642 cm^{-1}; uv max 323 mμ (ε 5500), 248 (23,000).

Anal. Calcd for $C_{15}H_{11}ClN_2O$: C, 66.55; H, 4.10; N, 10.35. Found: C, 66.37; H, 3.87; N, 10.18.

2,4-Diphenyl-1,3,5-benzoxadiazepine (2b).—Crystallization of the residue from irradiation of **1b** from ether gave 8.3 g of **2b**, mp 130–137°. Recrystallization from 2-propanol gave yellow needles: mp 135–137.5°; ir 1642 cm^{-1}; uv max 343 mμ (ε 3000), 266 (36,500); mass spectrum m/e 298, 195, 167.

Anal. Calcd for $C_{20}H_{14}N_2O$: C, 80.52; H, 4.73. Found: C, 80.70; H, 4.97.

1-Acetyl-5-chloro-3-phenylindazole (6). A. From Photolysis of 6-Chloro-2-methyl-4-phenylquinazoline 1-Oxide (4).—A solution of 7 g of **4** in 1.4 l. of benzene was irradiated with the Hanovia lamp for 6 days and then concentrated *in vacuo*. The residue was slurried with a mixture of hexane and ether, collected, and then washed with methanol to give 2.1 g of crude product, mp 120–135°. Recrystallization from ethyl acetate gave off-white needles: mp 157–159°; ir 1720 cm^{-1}; uv max 313 mμ (ε 13,500), 247 (sh) (26,000), 228 (30,400); mass spectrum m/e 270 (M^+), 228 (M − 42).

Anal. Calcd for $C_{15}H_{11}ClN_2O$: C, 66.55; H, 4.10; N, 10.35. Found: C, 66.79; H, 4.02; N, 10.26.

B. From Acetylation of 5-Chloro-3-phenylindazole.—A solution of 4.6 g of 5-chloro-3-phenylindazole[13] in 20 ml of pyridine was cooled in an ice bath and treated with 2 ml of acetyl chloride. After standing at room temperature for 2 hr the reaction mixture was diluted to 100 ml with water and the solid collected. Recrystallization from ethyl acetate gave 3.5 g of **6**, mp 155–159°, identified by mixture melting point, infrared spectrum, and thin layer chromatogram.

Irradiation of 7-Chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-Oxide (9).—A solution of 10 g of **9** in a mixture of 400 ml of ethanol and 1 l. of benzene was irradiated for 18 hr with the Hanovia lamp. The solution was concentrated *in vacuo*, and the residue crystallized from ether to give 5 g of a mixture of two photoisomers **11** and **12a** as judged by tlc, mp 165–170°. Recrystallization of a portion of this mixture three times from

(9) S. C. Bell and S. J. Childress, *J. Org. Chem.*, **29**, 506 (1964).
(10) L. S. Kaminsky and M. Lamchen, *J. Chem. Soc., C*, 2295 (1966).

(11) All melting points were determined in capillaries and are corrected. The ultraviolet spectra were determined in 2-propanol on a Cary Model 14 spectrophotometer, the nmr spectra on a Varian A-60 instrument, and the infrared spectra (in chloroform solution unless otherwise noted) on a Beckman IR-9 spectrophotometer. Thin layer chromatography was done on silica gel G plates using 5% methanol in chloroform or ethyl acetate as developer.
(12) J. T. Edward, *J. Chem. Soc.*, 222 (1956).
(13) K. Dziewonski and L. Sternbach, *Bull. Intern. Acad. Polon. Sci., Classe Med.*, **A333** (1935); *Chem. Abstr.*, **30**, 2972[4] (1936).

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[6] 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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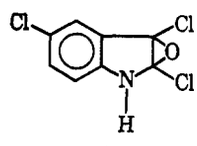
Contrary to literature reports, the major product of reaction of N,N-dichlorourethan (DCU) with indole and indole-2- or -3-carboxylic acid is 3,3,5-trichlorooxindole (**5**). Reaction of the methyl esters with DCU yields 2-carbomethoxy-2,5,7-trichloroindoxyl (**8**) and 3-carbomethoxy-3,5-dichlorooxindole (**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.

Aside from the apparent failure of **1** to undergo facile halogen migration, as 2-chloro epoxides are prone to



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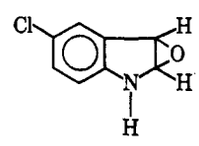

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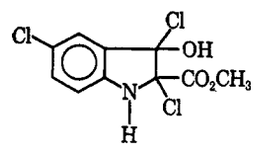

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do,[5] it was surprising that reduction was claimed to yield the dihydro product, 5-chloro-2,3-epoxyindoline

(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).