Quinazolines and 1,4-Benzodiazepines. XLIX.[1] Reactions of Oxaziridines with Amines

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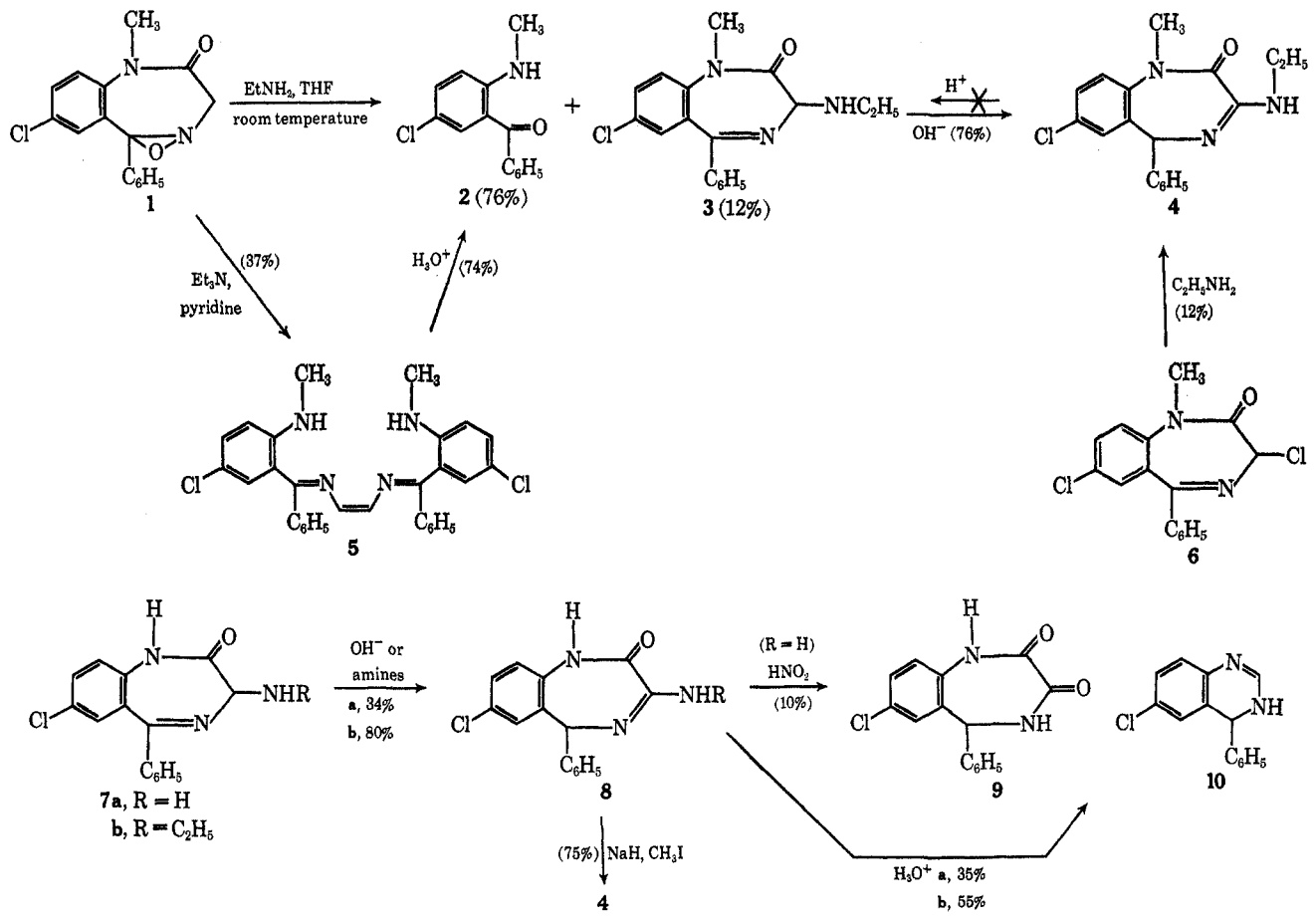
The reaction of 7-chloro-4,5-epoxy-1-methyl-5-phenyl-1,3,4,5-tetrahydro-2*H*-1,4-benzodiazepin-2-one (1) with ethylamine gave a mixture of 7-chloro-1,3-dihydro-3-ethylamino-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one (3) and 5-chloro-2-methylaminobenzophenone (2). Treatment of 1 with triethylamine in pyridine gave 1,2-bis(5-chloro-2-methylaminodiphenylmethyleneamino)ethylene (5). Reaction of the 1*H* analog of 1 (11) with ethylamine gave 2′-benzoyl-4′-chloro-2-ethyliminoacetanilide (12). The structures of 3, 5, and 12 were correlated by chemical conversions. Mechanisms for their formations are postulated. A base-catalyzed shift of the 4,5 double bond in 3 to give the amidine 4 was observed. The unusual dimeric structure 5 was confirmed by X-ray crystallographic analysis.

We recently prepared some readily isolable oxazirinobenzodiazepinones of type 1 and 11[2,3] and reported on the alcoholyses of 11 under mild conditions.[3] Since the reaction of *N*-alkyloxaziridines[4] with amines has not been reported in the literature,[5] we wish to present the results of our study on this type of reaction.

(1)[3] reacts with ethylamine in tetrahydrofuran at room temperature giving the 3-ethylaminolactam 3 (12%) and the amino ketone 2 (76%). In order to prove the structure of 3, we attempted to synthesize it from the 3-chlorolactam 6, a procedure by which several 3-alkylamino-7-chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodi-



We have found that 7-chloro-4,5-epoxy-1-methyl-5-phenyl-1,3,4,5-tetrahydro-2*H*-1,4-benzodiazepin-2-one

azepin-2-ones have been prepared from the desmethyl analog of 6.[6] We found that the reaction of 6 with ethylamine was very sluggish. After 20 days at room temperature only compound 4 could be obtained in 12% yield. The same product was formed quite readily (76%) from compound 3 by treatment with alkali. Attempts to reverse the reaction 4 → 3 using acetic acid and mineral acids failed. In order to prove the struc-

(1) Paper XLVIII: G. F. Field, W. J. Zally, and L. H. Sternbach, *J. Org. Chem.*, **36**, 777 (1971).

(2) R. Y. Ning, G. F. Field, and L. H. Sternbach, *J. Heterocycl. Chem.*, **7**, 475 (1970).

(3) R. Y. Ning, I. Douvan, and L. H. Sternbach, *J. Org. Chem.*, **35**, 2243 (1970).

(4) For a recent review, see J. F. Dupin, *Bull. Soc. Chem. Fr.*, 3085 (1967).

(5) The reaction of some *N*-acyl- and *N*-carbamoyloxaziridines with amines have been reported: E. Schmitz, S. Schramm, and R. Ohme, *J. Prakt. Chem.*, **36**, 86 (1967); *Chem. Ber.*, **100**, 2600 (1967).

(6) (a) S. C. Bell, R. J. Mc Caully, and S. J. Childress, *J. Org. Chem.*, **33**, 216 (1968); (b) S. C. Bell, R. J. Mc Caully, C. Gochman, S. J. Childress, and M. I. Gluckman, *J. Med. Chem.*, **11**, 457 (1968).

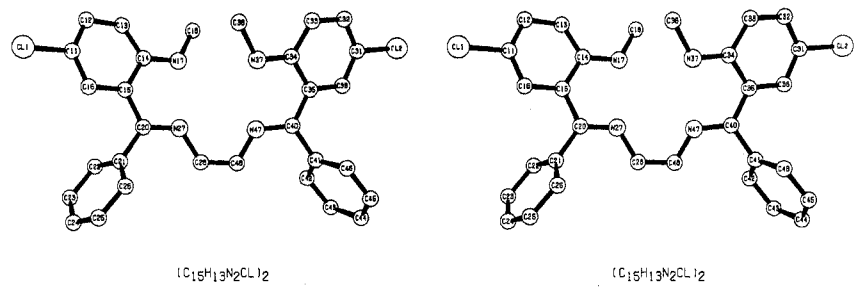
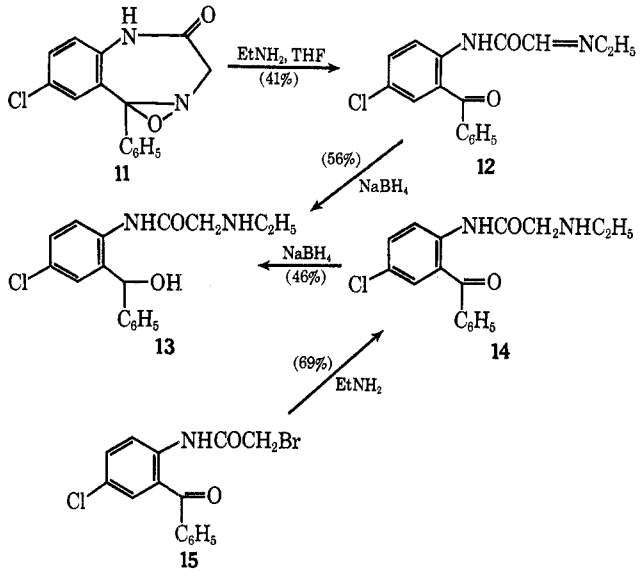


Figure 1.—Stereoscopic picture of 1,2-bis(5-chloro-2-methylaminodiphenylmethyleneamino)ethylene (5) obtained from X-ray crystallographic analysis. For details, see ref 9.

ture of 4 and its unexpected[6,7] formation from 3, we studied the behavior of the 1-*H*-3-alkylamino compounds 7a and 7b.[6] These compounds also isomerize in the presence of hydroxide ions or amines to 8a and 8b. Deamination by diazotization of 8a gave the known[8] dione 9, whereas methylation of 8b with sodium hydride and methyl iodide gave 4 in good yield. At room temperatures, 8a and 8b are relatively stable toward aqueous mineral acids. On heating with acid, however, the known dihydroquinazoline 10, a ring contraction product[8] of the dione 9, was obtained.

In contrast to 1, the demethyloxazirinobenzodiazepinone 11 gave, on treatment with ethylamine, as a



major product (41%), the ring-opened product 12. Its structure was established by reduction with sodium borohydride to the amino alcohol 13 and identification of the latter compound with the product prepared from 15 *via* 14 as shown below. Treatment of 1 with pyridine containing triethylamine yielded 5 as deep red colored needles in 37% yield. The dimeric nature of 5 was suggested by the mass spectrum. The molecular ion appeared at *m/e* 512 (calcd 512), with satellite peaks indicating the presence of two chlorine atoms. Hydrolysis in acid gave, in good yield, 5-chloro-2-methylaminobenzophenone (2). As a final proof the red crystals of 5 were submitted for X-ray crystallographic analysis. This analysis[9] unequivocally confirmed our assigned structure. The molecules, as shown in the stereoscopic picture (Figure 1), assume an interesting cis configuration about the central double bond.

Discussion

In Scheme I, we propose some plausible mechanisms leading to the observed products. The first step (I → II) involving deprotonation in the α position accompanied by cleavage of the N–O bond to give an alcoholate anion has been proposed earlier in the base-catalyzed decomposition of certain oxaziridines.[10] In the case of the ion derived from 1 (II, R = CH_3), the alcoholate anion reacts to a large extent intramolecularly with the carbonyl group, cleaving the amide bond (path a), and leading eventually to the main reaction product 2. A smaller part of II proceeds *via* path b leading to 3 (VIII, R = CH_3). The difference in the course of the aminolysis of 11 may be explained on the basis that the corresponding alcoholate anion in II (R = H) is quenched by proton exchange with the amide hydrogen thus protecting the amide linkage. The intermediate IV (R = H) then transforms *via* intermediates such as V and VI leading to 12 (VII, R = H).

Attempts to explain the formation of 5 led to speculation on the possible existence of the resonance-stabilized diradical IX resulting from the loss of carbon dioxide from III. Dimerization of IX gives 5. Although only the cis isomer is isolated (37%), the presence of the trans isomer in the reaction mixture is not precluded. Alternatively, the dimer X may form from III, followed by elimination of 2 mol of carbon dioxide to give 5. This, however, is only possible if the oxazolone III should undergo a thermal dimerization in a head-to-head manner.

(7) For an example of the isomerization of the double bond in the reverse direction (3,4 → 4,5) in these systems, see (a) S. C. Bell, R. J. Mc Caully, and S. J. Childress, *J. Med. Chem.*, **11**, 172 (1968); (b) R. I. Fryer, D. Winter, and L. H. Sternbach, *J. Heterocycl. Chem.*, **4**, 355 (1967).

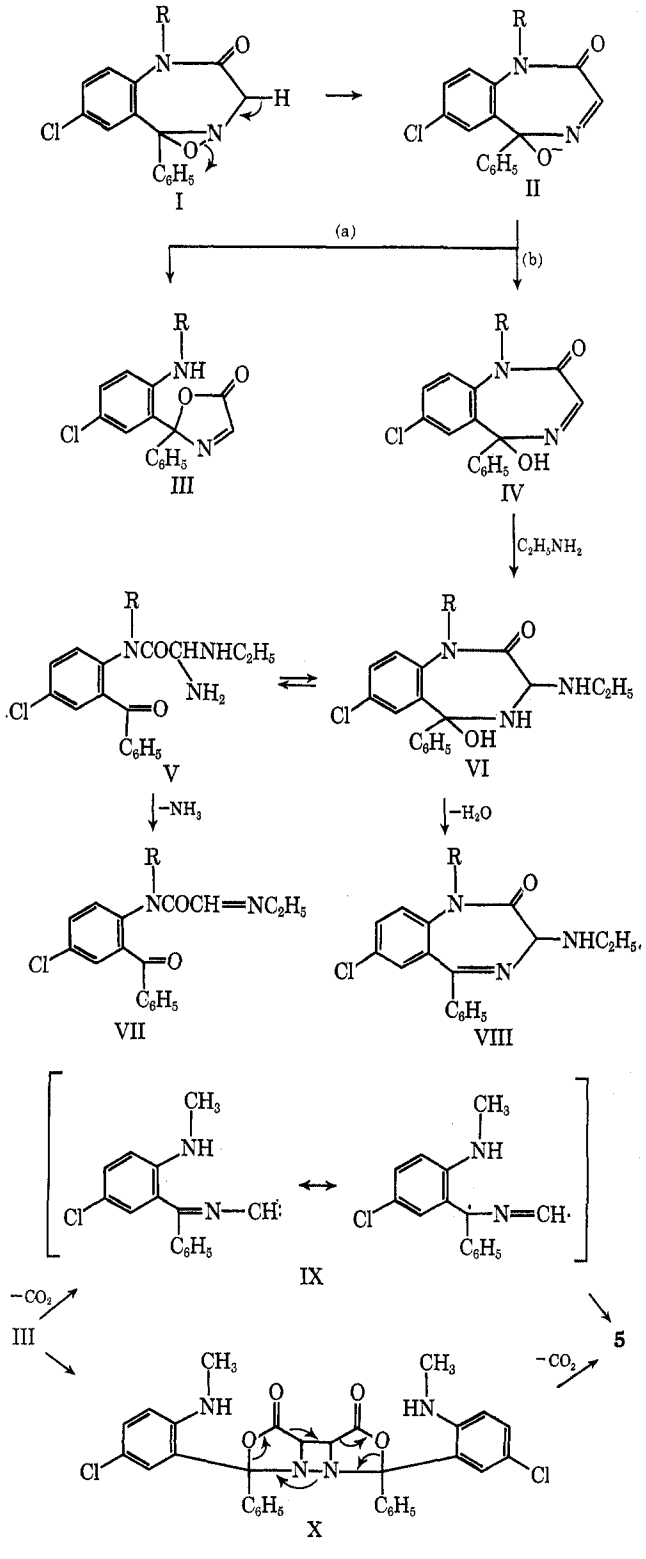
(8) S. C. Bell and S. J. Childress, *J. Org. Chem.*, **27**, 1691 (1962).

(9) This crystallographic analysis was conducted in our physicochemical laboratories by Dr. J. F. Blount. Crystals were obtained as described in the Experimental Section. We are grateful to Dr. Blount for the following summary of his results.

Compound **5** crystallizes in the triclinic space group $P\bar{1}$; the crystal data are a = 13.06, b = 10.26, c = 10.24 Å, α = 104.3°, β = 102.5°, γ = 86.0°, d_{expt} = 1.32 g cm^{-3}, d_{calcd} = 1.31 g cm^{-3} for Z = 2. Three-dimensional intensity data were measured on a Hilger-Watts Y290 four-circle diffractometer using nickel filtered Cu Kα radiation. The structure was solved by the heavy-atom method and refined by block diagonal least squares. The unweighted R value is 5.9% for an anisotropic model not including hydrogen atoms. The central C=C bond distance is 1.32 Å, the adjacent C–N distances are 1.38 and 1.41 Å, and the NC=CN torsion angle is 1°

(10) W. D. Emmons in "Heterocyclic Compounds with Three and Four Membered Rings," Part 1, A. Weissberger, Ed., Interscience, New York, N. Y., 1964, Chapter IV.

SCHEME I



Experimental Section[11]

Reaction of 1 with Ethylamine. 5-Chloro-2-methylaminobenzophenone (2) and 7-Chloro-1,3-dihydro-3-ethylamino-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one (3).—A solution of 3.01 g (10 mmol) of 7-chloro-4,5-epoxy-1-methyl-5-phenyl-1,3,4,5-tetrahydro-2*H*-1,4-benzodiazepin-2-one[3] in 20 ml of 1.46 *M* ethylamine in tetrahydrofuran was stirred at room temperature for 3 hr. The reaction mixture was evaporated to dryness. Crystallization of the residue from acetonitrile gave 394 mg (12%) of **3** as colorless prisms, mp 206–208°. After recrystallization from acetonitrile, an analytical sample, mp 214–215°, was obtained: uv max (EtOH) 227 mμ (ε 30,600), 260 (shoulder 13,200), and 312 (2350); ir (KBr) 3330 (weak, NH) and 1670 cm^{-1} (amide); nmr ($CDCl_3$) δ 4.34 ppm (s, 1, C_3-H); molecular ion *m/e* 327 (calcd 327).

Anal. Calcd for $C_{18}H_{18}ClN_3O$: C, 65.95; H, 5.53; N, 12.81; Cl, 10.81. Found: C, 66.03; H, 5.56; N, 12.69; Cl, 10.87.

The acetonitrile mother liquor containing the remaining product was evaporated to dryness. The residue was dissolved in a small volume of ether and applied to a column of 50 g of neutral alumina (Woelm, activity I). The column was eluted with hexane until the effluent showed no yellow color (about 1.5 l.). Upon concentration of the hexane solution to a small volume followed by standing, 1.86 g (76%) of **2**, mp 94–96°, was obtained. The infrared spectrum was identical with that of an authentic sample.[12]

7-Chloro-1,5-dihydro-3-ethylamino-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one (4). A. From 6.—A solution of 1.00 g (3.04 mmol) of **6** in 40 ml of 2.3 *M* ethylamine in tetrahydrofuran was allowed to stand at room temperature for 20 days. The solution was evaporated to dryness. The residue was partitioned between methylene chloride and saturated brine. The methylene chloride layer was dried (Na_2SO_4) and evaporated. Solution of the residue in ether gave, on standing, 120 mg (12%) of **4** as a light yellow powder, mp 220–222°. After recrystallization from acetonitrile, light yellow plates were obtained: mp 226–227.5°; uv max 213 mμ (ε 30,000), 240 (shoulder, 14,700), and 290 (shoulder, 5000); ir (KBr) 3380 (very strong, NH), 1650 (C=O), and 1620 cm^{-1} (C=N); nmr ($CDCl_3$) δ 5.68 ppm (s, 1, C_5-H).

Anal. Calcd for $C_{18}H_{18}ClN_3O$: C, 65.95; H, 5.53; N, 12.81; Cl, 10.81. Found: C, 65.96; H, 5.50; N, 12.84; Cl, 10.95.

B. From the Isomerization of 3.—To a solution of 300 mg (0.89 mmol) of **3** in 50 ml of tetrahydrofuran was added 0.5 mmol of benzyltrimethylammonium hydroxide (as 40% solution in methanol). The mixture was stirred for 24 hr at room temperature and the solvent was evaporated. The residue was partitioned between methylene chloride and saturated brine. The methylene chloride layer was washed once with brine, dried (Na_2SO_4), and evaporated. The residue crystallized from acetonitrile affording 228.5 mg (76%) of **4**, mp 224–225°. The infrared spectrum of this material was identical with that prepared by method A above.

C. From Methylation of 8b.—To a solution of 220 mg (0.70 mmol) of **8b** in 10 ml of tetrahydrofuran was added 40 mg (0.84 mmol) of 50% oil dispersion of sodium hydride. This mixture was stirred at room temperature for 30 min. Excess methyl iodide (1.0 ml, 15 mmol) was added in one portion. After 1 hr, the reaction mixture was evaporated to dryness. The residue was partitioned between methylene chloride and saturated brine. The methylene chloride layer was dried (Na_2SO_4) and evaporated. Crystallization of the residue from acetonitrile gave 127 mg (75%) of **4**, mp 222–224°, and was identical with the material prepared by methods A and B above (mixture melting point, ir, tlc).

1,2-Bis(5-chloro-2-methylaminodiphenylmethyleneamino)-ethylene (5).—To a solution of 1.504 g (5.00 mmol) of 1[3] in 10 ml of pyridine was added 1.0 ml of triethylamine. The solution was allowed to stand at room temperature for 2 hr and then evaporated to near dryness. The residue was partitioned between methylene chloride and saturated brine. The methylene chloride layer was dried (Na_2SO_4) and evaporated. Crystallization of the residue from acetonitrile afforded 470 mg (37%) of **5** as deep red needles, mp 205–207°. Recrystallization from acetonitrile gave mp 208–209.5°; uv max (*i*-PrOH) 233 mμ (ε 17,800), 244 (8350), and 475 (6000); ir (KBr) 3200 (NH), 1600–1500 cm^{-1} (complex bands); molecular ion *m/e* 512 (calcd 512), containing two chlorine atoms.

(11) All melting points were taken in a Thomas-Hoover melting point apparatus and are corrected. Infrared spectra were taken on a Beckman IR-9 or a Perkin-Elmer 621 grating spectrophotometer, mass spectra on a CEC-21-110 spectrometer, nuclear magnetic resonance spectra on a Varian A-60 spectrometer using tetramethylsilane as internal standard, and ultraviolet spectra on a Cary 14M or 15 recording spectrophotometer. All spectra obtained are compatible with the structures assigned. For brevity, only some crucial data are selected from these spectra and reported here. All solvents used were of reagent grade purity. Ether refers to diethyl ether. All solvents were evaporated on a Büchi Rotavapor evaporator under water-aspirator pressure at a bath temperature of 30–40°, unless otherwise specified.

(12) L. H. Sternbach, R. I. Fryer, W. Metlesics, G. Sach, and A. Stempel, *J. Org. Chem.*, **27**, 3781 (1962).

Anal. Calcd for $C_{30}H_{26}Cl_2N_4$: C, 70.17; H, 5.10; N, 10.91; Cl, 13.81. Found: C, 70.40; H, 5.15; N, 11.13; Cl, 13.85.

Long needle-like red crystals suitable for X-ray crystallographic analysis were obtained by allowing a saturated solution of **5** in acetonitrile to stand at room temperature over several weeks.

Hydrolysis of 5.—A solution of 300 mg (0.590 mmol) of **5** in 30 ml of tetrahydrofuran was mixed with 20 ml of 1.5 *N* aqueous HCl. After the mixture was stirred overnight at room temperature, it was neutralized with a saturated aqueous solution of sodium bicarbonate. The product was isolated by extractions with methylene chloride. Crystallization from hexane afforded 210 mg (75%) of **2**, as yellow needles, mp 95–96°. The infrared spectrum was identical with that of an authentic sample.[13]

3,7-Dichloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one (6).—This procedure is a modification of that reported[6,8] for the preparation of the 1-H analog of **6**.

To 5.00 g (16.7 mmol) of 7-chloro-1,3-dihydro-3-hydroxy-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one[5] was added 5 ml of thionyl chloride. The mixture was heated gently under nitrogen on a steam bath with periodic stirring for 30 min. The mixture attained a pasty consistency. Excess thionyl chloride was removed by washing by decantation with pentane. The residual yellow gum was treated with concentrated ammonium hydroxide and extracted with methylene chloride. The methylene chloride layer was washed with water, dried (Na_2SO_4), and evaporated. Crystallization of the residue from ether gave 3.50 g (64%) of **6**: colorless prisms, mp 108–110°; ir (KBr) 1690 cm^{-1} (amide); uv max (EtOH) 230 mμ (ε 29,000) 255 (14,700), and 312 (2400).

Anal. Calcd for $C_{16}H_{12}Cl_2N_2O$: C, 60.21; H, 3.79; N, 8.77. Found: C, 60.36; H, 4.07; N, 8.49.

7-Chloro-1,3-dihydro-3-ethylamino-5-phenyl-2*H*-1,4-benzodiazepin-2-one (7b).—To 5.00 g (17.4 mmol) of 7-chloro-1,3-dihydro-3-hydroxy-5-phenyl-2*H*-1,4-benzodiazepin-2-one[8] was added 8 ml of thionyl chloride. This mixture was heated gently on a steam bath, with periodic stirring, for 30 min. The mixture attained a pasty consistency. The excess thionyl chloride was removed by washing by decantation with pentane. To the residue was added 180 ml of 2.3 *M* ethylamine in tetrahydrofuran. This mixture was stirred at room temperature for 1 hr. Salts were removed by filtration. The filtrate was evaporated to dryness. Crystallization of the residue from acetonitrile gave 2.67 g (49%) of **7b**, mp 195–197°. Recrystallizations from acetonitrile gave colorless prisms: mp 199–200°; uv (CH_3CN) 225 mμ (ε 37,350) and 312 (2340); ir (KBr) 1690 cm^{-1} (amide); nmr (DMSO-d_6) δ 4.17 ppm (s, 1, C_3-H).

Anal. Calcd for $C_{17}H_{16}ClN_3O$: C, 65.07; H, 5.14; N, 13.39; Cl, 11.30. Found: C, 65.12; H, 5.18; N, 13.46; Cl, 11.51.

3-Amino-7-chloro-1,5-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one (8a).—To a solution of 500 mg (1.93 mmol) of 3-amino-7-chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one[6a] in 50 ml of tetrahydrofuran was added 2.1 mmol of benzyltrimethylammonium hydroxide (as 40% solution in methanol). This mixture was heated to reflux for 30 hr and the solvents were evaporated. The residue was partitioned between methylene chloride and saturated brine. The methylene chloride layer was dried and evaporated to dryness. The residue was crystallized from acetonitrile affording 168 mg (34%) of **8a** as a colorless, amorphous solid: mp 274–275° dec; uv max (CH_3CN) 213 mμ (shoulder, ε 32,000), 252 (13,000), and 295 (shoulder, 3000); ir (KBr) 3450 and 3350 (NH_2), 1670 (C=O), and 1630 cm^{-1} (C=N); nmr (DMSO-d_6) δ 5.40 ppm (s, 1, C_5-H).

Anal. Calcd for $C_{15}H_{12}ClN_3O$: C, 63.05; H, 4.23; N, 14.71; Cl, 12.41. Found: C, 62.92; H, 4.25; N, 14.68; Cl, 12.36.

Diazotization of 8a. 7-Chloro-5-phenyl-1,3,4,5-tetrahydro-2*H*-1,4-benzodiazepine-2,3-dione (9).[8]—To a warm solution (50–60°) of 800 mg (2.81 mmol) of **8a** in 16 ml of 0.50 *N* aqueous HCl was added, dropwise, a solution of 240 mg (3.48 mmol) of sodium nitrite in 5 ml of water. Solids precipitated immediately. After 15 min, the precipitate was collected on a filter and washed with water. Recrystallization of this solid from ethanol gave 56.5 mg (10% based on unrecovered **8a** some of which was recovered as described below) of **9** as prisms, mp 290–292°. The infrared spectrum of this material was identical with that of an authentic sample prepared by sodium hydroxide catalyzed tautomerism[8] of 7-chloro-1,3-dihydro-3-hydroxy-5-phenyl-2*H*-1,4-benzodiazepin-2-one.

(13) L. H. Sternbach, R. I. Fryer, W. Metlesics, E. Reeder, G. Sach, G. Saucy, and A. Stempel, *J. Org. Chem.*, **27**, 3788 (1962).

The aqueous filtrate portion of the reaction mixture was neutralized with sodium bicarbonate. Unchanged **8a** (266 mg) precipitated and was identified by tlc and comparison of infrared spectra.

Hydrolysis of 8a.—A solution of 370 mg (1.29 mmol) of **8a** in 100 ml of 2.0 *N* HCl was heated on a steam bath for 32 hr. The solid that precipitated in this period was collected (260 mg). It was dissolved in a small volume of dimethylformamide and reprecipitated by the addition of saturated brine. The precipitate was collected, washed with water, and dried. After recrystallization from ether–petroleum ether, 170 mg (55%) of 6-chloro-3,4-dihydro-4-phenylquinazoline (**10**)[8] was obtained as colorless prisms, mp 171–173°. It was found to be identical (mixture melting point, ir) with a sample prepared by the known procedure.

7-Chloro-1,5-dihydro-3-ethylamino-5-phenyl-2*H*-1,4-benzodiazepin-2-one (8b).—A solution of 200 mg (0.65 mmol) of **7b** in 50 ml of 1.4 *M* ethylamine in tetrahydrofuran was allowed to stand at room temperature for 12 days. Only a trace of starting material remained (tlc). The solution was evaporated. Crystallization of the residue from acetonitrile gave 160 mg (80%) of **8b** as colorless needles: mp 208–209°; uv max (CH_3CN) 253 mμ (shoulder, ε 11,300) and 293 (shoulder 4500); ir (KBr) 3430 (amidine NH), 3200 (amide NH), 1670 (C=O), and 1630 cm^{-1} (C=N); nmr ($CDCl_3$) δ 5.58 (s, 1, C_5-H), 3.34 ppm (m, 2, CH_2CH_3, collapsed to quartet after exchange with deuterium oxide).

Anal. Calcd for $C_{17}H_{16}ClN_3O$: C, 65.07; H, 5.14; N, 13.39; Cl, 11.30. Found: C, 65.11; H, 5.03; N, 13.38; Cl, 11.20.

Hydrolysis of 8b.—A solution of 300 mg (1.05 mmol) of **8b** in 50 ml of 2 *N* HCl was heated on a steam bath for 54 hr. The precipitate formed during this period was collected and treated in the same manner as described for the hydrolysis of **8a**. The yield of **10** was 90 mg (35%), mp 168–170°. The infrared spectrum of this material was identical with that obtained from **8a**.

2′-Benzoyl-4′-chloro-2-ethyliminoacetanilide (12).—A solution of 1.00 g (3.5 mmol) of 7-chloro-4,5-epoxy-5-phenyl-1,3,4,5-tetrahydro-2*H*-1,4-benzodiazepin-2-one[2] in 50 ml of 0.65 *N* (32.5 mmol) ethylamine in tetrahydrofuran was allowed to stand for 23 hr. Evaporation of solvents gave an oily residue which crystallized from ethanol, affording 448 mg (41%) of **12**, mp 94–95.5°. After recrystallization from ethanol, pale yellow needles were obtained: mp 95–96°; uv max (*i*-PrOH) 224 mμ (ε 17,900), 256 (17,200), and 337 (5900); ir (KBr) 3240 (NH), 1710 (amide), 1640 cm^{-1} (C=O); molecular ion *m/e* 314 (calcd 314); nmr (DMSO-d_6) δ 1.20 (t, 3, CH_3), 3.67 (q, 2, CH_2), 7.4–8.4 (m, 9, aromatic and CH=N), and 11.10 ppm (s, 1, NH).

Anal. Calcd for $C_{17}H_{15}ClN_2O_2$: C, 64.87; H, 4.80; N, 8.90; Cl, 11.26. Found: C, 64.76; H, 4.74; N, 8.74; Cl, 11.27.

5-Chloro-2-(2-ethylaminoacetamido)benzhydrol (13). A. From 12.—To a solution of 313 mg (1.0 mmol) of **12** in 40 ml of ethanol was added 57 mg (1.5 mmol) of sodium borohydride. The mixture was stirred at room temperature overnight. Ethanol was evaporated. The residue was partitioned between methylene chloride and brine. The methylene chloride layer was dried (Na_2SO_4) and evaporated. Crystallization from ether–hexane gave 180 mg (56%) of **13** as colorless needles: mp 109–110°; uv max (*i*-PrOH) 254 mμ (ε 15,200) and 293 (shoulder, 800); ir (KBr) 3300 and 3200 (broad, OH, NH) and 1660 cm^{-1} (amide); molecular ion *m/e* 318 (calcd 318); nmr ($CDCl_3$) δ 3.15 (s, 2, $COCH_2$) and 5.83 ppm (s, 1, CHO).

Anal. Calcd for $C_{17}H_{19}ClN_2O_2$: C, 64.05; H, 6.01; N, 8.79; Cl, 11.12. Found: C, 63.84; H, 5.94; N, 8.76; Cl, 11.20.

B. From 14.—To a solution of 318 mg (1.0 mmol) of **14** in 20 ml of ethanol was added 57 mg (1.5 mmol) of sodium borohydride. This mixture was stirred for 3 hr at room temperature. The product was isolated and recrystallized in the same manner as described in A. The yield of **13** was 148 mg (46%), mp 110–111°. This material is identical (mixture melting point, ir, tlc) with that obtained from **12**.

2′-Benzoyl-4′-chloro-2-ethylaminoacetanilide (14).—A solution of 35.2 g (100 mmol) of 2′-benzoyl-4′-chloro-2-bromoacetanilide[13] in 400 ml of 1.45 *M* ethylamine was allowed to stand at room temperature for 6 hr. The precipitated solid was removed by filtration. The filtrate was evaporated. The residue was partitioned between methylene chloride and brine. The methylene chloride layer was dried (Na_2SO_4) and evaporated. Crystallization of the residue from hexane afforded 21.1 g (69%) of **14**

as colorless needles: mp 80–81°; uv max (*i*-PrOH) 240 mμ (ε 29,300), 265 (shoulder, 14,500), and 333 (3900); ir (KBr) 3200 and 3330 (NH), 1675 (amide), and 1650 cm^{-1} (C=O); molecular ion *m/e* 316 (calcd 316); nmr ($CDCl_3$) δ 3.39 ppm (s, 2, $COCH_2$).

Anal. Calcd for $C_{17}H_{17}ClN_2O_2$: C, 64.45; H, 5.41; N, 8.84; Cl, 11.19. Found: C, 64.41; H, 5.59; N, 8.85; Cl, 11.38.

Registry No.—**3**, 27723-27-9; **4**, 27723-28-0; **5**, 27729-86-8; **6**, 23433-96-7; **7b**, 27723-30-4; **8a**, 27723-31-5; **8b**, 27669-87-0; **12**, 27723-32-6; **13**, 27723-15-5; **14**, 27723-16-6.

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Reaction of 2,3-Dialkylaziridines with Carbon Disulfide

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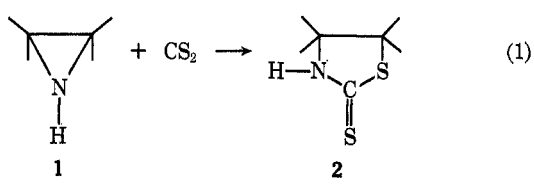
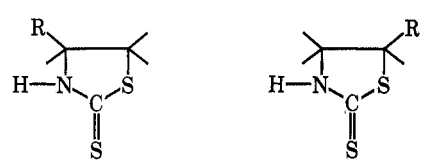
The reaction of *cis*- and *trans*-2,3-dialkyl-substituted aziridines with carbon disulfide to yield 4,5-disubstituted thiazolidine-2-thiones has been studied. The yields of the thiazolidinethiones are in the range of 30–80%. The geometric configurations of the thiazolidinethiones have been elucidated by means of nmr and mass spectroscopy. It has been found that the thiazolidinethiones have the opposite geometry as the starting aziridines. Starting with a *cis*-aziridine yields a *trans*-thiazolidinethione, while the *trans*-aziridine yields the corresponding *cis*-thiazolidinethione. The reaction has been determined to be stereospecific for *cis*-aziridines but only stereoselective for *trans*-aziridines. Also studied was the reaction of 2-alkyl-substituted aziridines with carbon disulfide. The products from this reaction were found to be 4-alkyl-substituted thiazolidine-2-thiones.

The reaction of ethylenimine (**1**) with carbon disulfide to give thiazolidine-2-thiones (**2**) (eq 1) was initially



(1)

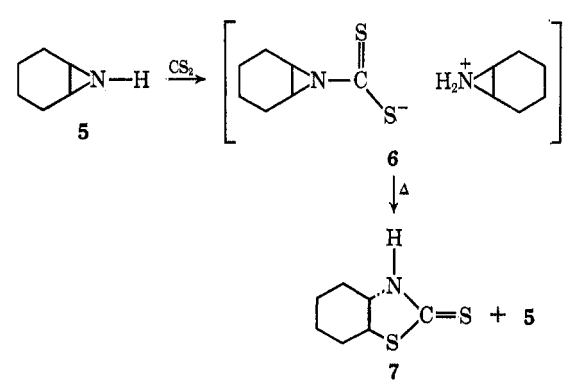
1 **2**



3, R = alkyl **4**, R = aryl

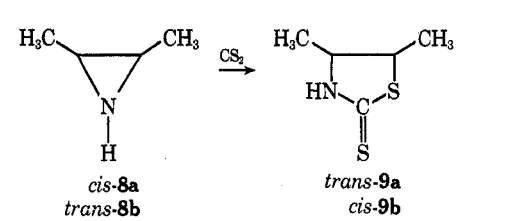
reported by Gabriel, *et al.*[1,2] The scope of this reaction was later extended by Clapp, *et al.*,[3] to include alkyl-substituted ethylenimines. These authors found that the reaction of 2-alkylaziridines with carbon disulfide yielded the corresponding 4-alkylthiazolidine-2-thione derivatives (**3**), thus establishing that for alkyl-substituted aziridines the three-membered ring is opened preferentially at the least substituted carbon atom. Similar orientation results have also been observed with *N*-alkyl- and *N*-aryl-2-alkylaziridines.[4,5] More recently, Kotera, *et al.*,[6] utilized this reaction for the derivatization of a number of 2-aryl-substituted aziridines. The thiazolidine-2-thiones so prepared were described as the 5-substituted isomers (**4**), thus indicating that the aziridine ring had been opened at the position bearing the aryl substituent.

With cyclohexylimine (**5**) Winternitz, *et al.*,[7] observed the formation of perhydrobenzo-4,5-thiazolidine-2-thione (**7**) whose stereochemistry about the ring junction was definitively assigned as trans. An isolated intermediate from this reaction was assigned the aziridinium dithiocarbamate structure **6** which was found to liberate the thiazolidinethione and cyclohexylimine on pyrolysis (eq 2). The stereochemical outcome of this reaction has also been suggested by Dewey, *et al.*,[8] who studied this reaction with *cis*- and *trans*-2,3-dimethylaziridine (**8a** and **8b**). The thiazolidine-2-thiones obtained from these aziridines were assigned the trans and cis geometry (**9a** and **9b**), respectively (eq 3).



5 **6** **7**

(2)



(3)

cis-**8a** *trans*-**9a**
trans-**8b** *cis*-**9b**

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