phenanthridine, m.p. 103–104°. A mixture melting point with authentic material prepared as described[19] showed m.p. 103–105°. The infrared spectra of the two compounds were superimposable.

Decarboxylation of II to Give I.—A mixture of 1 g. of II and 1 g. of copper powder in 25 ml. of quinoline was heated under reflux for 3 hr. The mixture was filtered, 50 ml. of chloroform was added, and the organic phase was washed in turn with *N* hydrochloric acid and water. The organic phase was dried and the solvent was removed. The yellow solid was recrystallized from acetic acid to give 0.6 g. (75%) of I, m.p. 235–238°. A mixture melting point with I showed no depression.

Thermal Rearrangement of II.—When II was heated in mesitylene at 278° for 5 days an acid (V) which did not melt below 360° was obtained. The infrared spectrum of this acid was identical with that of the acid obtained by hydrolysis of VI.

Anal. Calcd. for $C_{21}H_{13}NO_4$: C, 73.46; H, 3.82; N, 4.08. Found: C, 73.09; H, 3.78; N, 3.98.

Decarboxylation of V to IV.—The acid V, 60 mg., and 100 mg. of copper powder in 2 ml. of quinoline were refluxed 3 hr. After filtration the quinoline was removed by heating *in vacuo* and the residue was recrystallized from ethanol to give 10 mg., of solid, m.p. 103–106°. The melting point was undepressed when mixed with authentic 9-phenylphenanthridine.[19]

Preparation and Thermal Rearrangement of Benzil Dianil.—A mixture of 4.2 g. of benzil, 4 g. of aniline, 0.5 g. of *p*-toluenesulfonic acid, and 60 ml. of toluene was heated under reflux for 2 days. The water which was formed from the reaction was removed with a water separator.

The cooled solution was filtered to remove the *p*-toluenesulfonic acid, and the solvent was removed *in vacuo*. The residues were recrystallized twice from an ether–pentane mixture, 5 g. (69%), m.p. 140–142° (lit.[20] m.p. 141–142°).

A solution of 100 mg. of benzil dianil in 20 ml. of mesitylene was heated in a sealed tube at 280° for 24 hr. Upon evaporation of the mesitylene only starting material (90 mg.) was isolated, m.p. 139–142°. A solution of 1 g. of benzil dianil and 20 ml. of benzene was heated in a sealed tube at 278° for 8 days. After the benzene was removed the residues were chromatographed on acid-washed alumina. The first product eluted with pentane was biphenyl (100 mg.), m.p. 68–76°, which was undepressed when mixed with an authentic sample. The second fraction contained about 50 mg. of benzaldehyde, characterized as its 2,4-dinitrophenylhydrazone, m.p. 236–237°. The third fraction (300 mg.), m.p. 139–142°, was eluted with a 50–50 pentane–ether mixture and was shown to be starting material by a mixture melting point determination. The largest fraction of material (500 mg.) was eluted with ether and appeared to be a noncrystalline polymer containing some starting material. The last product (about 5 mg.) was obtained by elution with methanol and was a deep purple water-soluble substance which was not characterized.

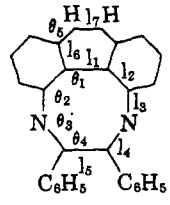
It was noted that, when the pure benzil dianil was heated above 400° in a small glass tube, traces of benzonitrile could be detected from the infrared spectrum of the distillate and by odor.

(19) A. Pictet and A. Hubert, *Ber.*, **29**, 1182 (1896).

(20) M. Siegfeld *Ber.* **25**, 2600 (1892).

Appendix

For the energy calculation, the initial geometry of the molecule in the planar form was assumed using normal bond lengths[21] and these minimally deformed angles.



l_1 1.520 Å.	θ_1 134°
l_2 1.390 Å.	θ_2 136°
l_3 1.475 Å.	θ_3 134°
l_4 1.350 Å.	θ_4 137°
l_5 1.450 Å	θ_5 120°
l_6 1.09 Å	
l_7 0.70 Å	

The stretching and bending constants used are those given by Westheimer[9] for the aromatic hydrogen and for ethylene. The ethylene bending constant was used in this calculation for all angles not involving the aromatic hydrogen. The energy of the system was minimized with respect to θ_1, θ_2, θ_3, θ_4, θ_5, l_6, and l_7, simultaneously and in the minimum energy form these quantities had the values: $\theta_1 = 129°$, $\theta_2 = 138°$, $\theta_3 = 141°$, $\theta_4 = 132°$, $\theta_5 = 111°$, $l_6 = 1.04$ Å., and $l_7 = 1.53$ Å.

(21) Tables of interatomic distances and configurations in molecules and ions, special publication no. 11, the Chemical Society, London (1958).

The Rearrangement of 2-Amino-5-phenyl-3*H*-1,4-benzodiazepine 4-Oxides with Acetic Anhydride

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2-Amino-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide (I) gave 2-acetamido-3-acetoxy-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine (II), 10-acetyl-7-chloro-2-methyl-5-phenyl-10*H*-oxazolo[4,5-*b*]-1,4-benzodiazepine (V), and 2-acetamido-7-chloro-5-phenyl-3*H*-1,4-benzodiazepin-3-one (VI) upon treatment with acetic anhydride under varying conditions. The structures of the products were established by chemical and spectroscopic evidence. The 2-methylamino analog of I also was studied.

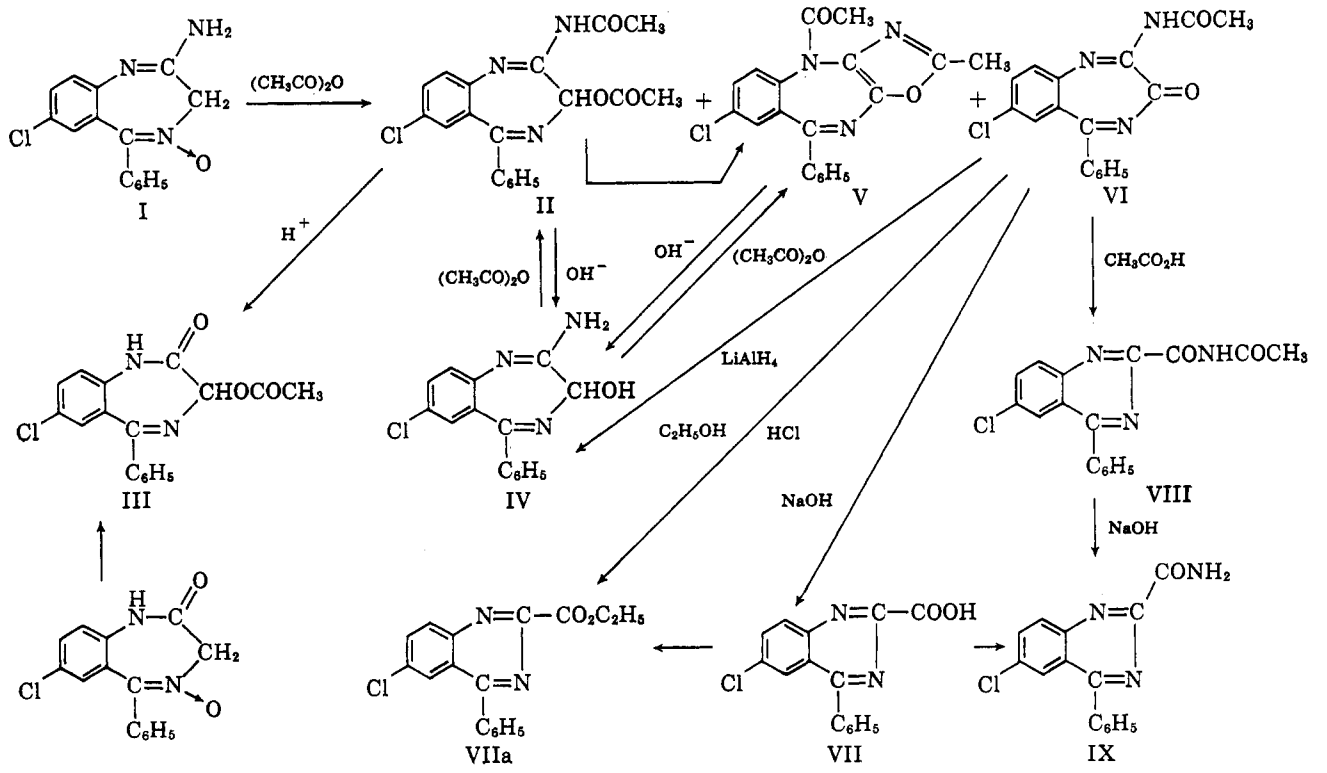
The rearrangement of 1,3-dihydro-5-aryl-2*H*-1,4-benzodiazepin-2-one 4-oxides[1] with acid anhydrides resulting in 3-acyloxy-1,3-dihydro-5-aryl-2*H*-1,4-benzodiazepin-2-ones recently has been reported from this laboratory.[2] In a similar manner, 2-amino-5-aryl-3*H*-1,4-benzodiazepine 4-oxides[3] have undergone rearrangements upon treatment with acid anhydrides. In some instances, however, several other products were isolated, the relative amounts often depending upon the conditions of the reactions.

The reaction of 2-amino-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide (I) with acetic anhydride gave three rearranged products (II, V, VI). 2-Acetamido-3-acetoxy-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine (II), the expected compound, was hydrolyzed

(1)(a) L. H. Sternbach and E. Reeder, *J. Org. Chem.*, **26**, 4936 (1961); (b) S. C. Bell, T. S. Sulkowski, C. Gochman, and S. J. Childress, *ibid.*, **27**, 562 (1962).

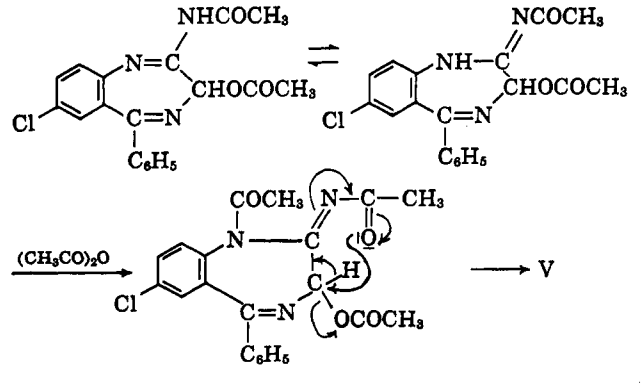
(2) S. C. Bell and S. J. Childress, *ibid.*, **27**, 1691 (1962).

(3)(a) L. H. Sternbach, U. S. Patent 2,893,992 (1959); (b) L. H. Sternbach and E. Reeder, *J. Org. Chem.*, **26**, 1111 (1961); and (c) S. C. Bell, C. Gochman, and S. J. Childress, *J. Med. Pharm. Chem.*, **5**, 63 (1962).



with dilute acid to the known 3-acetoxy-7-chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one[2] (III) and with alkali to 2-amino-7-chloro-3-hydroxy-5-phenyl-3*H*-1,4-benzodiazepine (IV).

The second product (V) of this reaction had an analysis corresponding to that of II minus the elements of water. Compound V also produced IV upon treatment with alkali. Compound IV, upon warming with acetic anhydride, was reacetylated to give II. The route (V → IV → II → III) proved the retention of the seven-membered ring in V and IV. Upon heating IV in acetic anhydride under reflux, V was formed. Compound V was stable to catalytic reduction and to acid. It absorbed in the infrared at 5.90 μ (C=O) and there were no bands corresponding to NH or OH. There were two methyl singlets in the n.m.r. spectrum (δ 2.25, 2.52).[4] Compound V was, therefore, assigned the structure 10 - acetyl - 7 - chloro - 2 - methyl - 5-phenyl - 10*H* - oxazolo[4,5 - *b*] - 1,4 - benzodiazepine. A plausible mechanism for its formation from II would be the acetylation of the tautomer of II followed by the elimination of acetic acid.



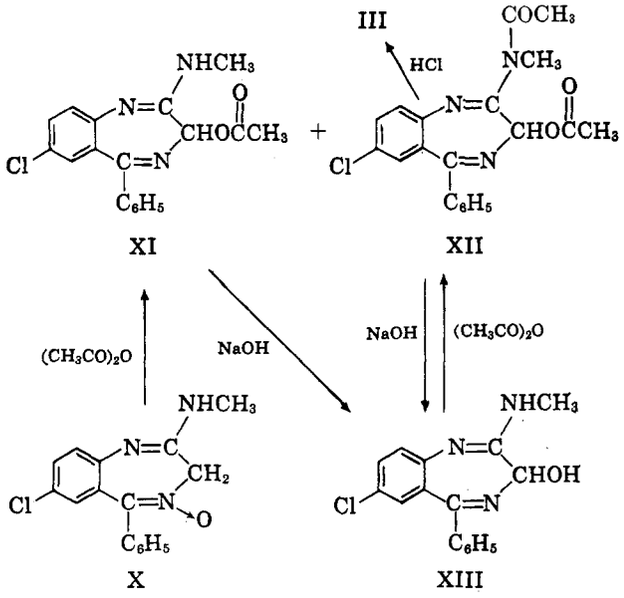
The third compound VI isolated from the original reaction had the empirical composition of the acetylated starting material (I) minus one mole of hydrogen. VI readily underwent a rearrangement and hydrolysis in cold dilute alkali to form 6-chloro-4-phenylquinazoline-2-carboxylic acid[2] (VII). In refluxing alcoholic hydrogen chloride, VI afforded the ethyl ester of VII. When heated with acetic acid, VI rearranged to the isomeric N-acetyl-6-chloro-4-phenylquinazoline-2-carboxamide (VIII). Compound VIII was further hydrolyzed to 6 - chloro - 4 - phenylquinazoline - 2-carboxamide (IX) with sodium hydroxide. IX was prepared unambiguously from VII for comparison. The conversion of VI to IV with lithium aluminum hydride confirmed the presence of the 1,4-benzodiazepine ring in VI. The infrared absorption spectrum of VI had two carbonyl bands (5.77, 5.88 μ), one of which was ascribed to the 2-acetamido group, and the second to a carbonyl group in the ring. From these transformations and infrared data as well as a consistent n.m.r. spectrum (methyl singlet, δ 2.14)[5] it was concluded that VI was 2-acetamido-7-chloro-5-phenyl-3*H*-1,4-benzodiazepin-3-one.

7 - Chloro - 2 - methylamino - 5 - phenyl - 3*H*-1,4-benzodiazepine 4-oxide (X) was heated with acetic anhydride under varying conditions. When heated at 100° for a short time there was obtained a monoacylated, rearranged compound, 3-acetoxy-7-chloro-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepine (XI). The infrared absorption at 5.72 μ suggested this structure instead of the possible alternative, 7-chloro-3-hydroxy - 2 - N - methylacetamido - 5 - phenyl - 3*H*-1,4-benzodiazepine. Heating either X or XI with acetic anhydride for an extended period of time produced the diacetylated compound, 3-acetoxy-2-N-methylacetamido - 7 - chloro - 5 - phenyl - 3*H* - 1,4-benzodiazepine (XII). Both XI and XII were con-

(4) The spectrum was determined in deuteriochloroform (tetramethylsilane standard) with a Varian A-60 spectrometer.

(5) Deuterio dimethyl sulfoxide.

verted into 7-chloro-3-hydroxy-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepine (XIII) by treatment with alkali. Compound XII was hydrolyzed in dilute hydrochloric acid to the corresponding benzodiazepin-2-one (III).



Experimental[6]

Reactions between I and Acetic Anhydride. A.—A mixture of 15 g. of I and 300 ml. of acetic anhydride was heated on the steam bath for 1.25 hr. The reaction mixture turned red. After cooling 3.0 g. of white VI, m.p. 239–240° (turned dark green), was filtered off.

Anal. Calcd. for $C_{17}H_{12}ClN_3O_2$: C, 62.67; H, 3.71; N, 12.90; Cl, 10.88. Found: C, 62.37; H, 3.70; N, 13.27; Cl, 10.60.

The filtrate from the reaction mixture was concentrated *in vacuo*, and the residue was recrystallized twice from ethanol giving 11.2 g. of II, yellow, m.p. 181–182°.

Anal. Calcd. for $C_{19}H_{16}ClN_3O_3$: C, 61.71; H, 4.36; N, 11.36; Cl, 9.59. Found: C, 61.94; H, 4.30; N, 11.45; Cl, 9.87.

B.—A mixture of 5.0 g. of I and 200 ml. of acetic anhydride was heated under reflux for 15 min. The reaction mixture became red. The solution was concentrated to one-third its volume *in vacuo*. After cooling there was obtained 1.75 g. of VI. The remainder of the acetic anhydride was removed *in vacuo*, and the residue was recrystallized twice from ethanol to afford V, yellow, m.p. 183–185°.

Anal. Calcd. for $C_{19}H_{14}ClN_3O_2$: C, 64.87; H, 4.01; N, 11.94; Cl, 10.08. Found: C, 64.66; H, 3.92; N, 11.86; Cl, 9.90.

C.—Compound II or IV was converted into V by heating in acetic anhydride under reflux for 0.5 hr., removing the solvent *in vacuo*, and recrystallizing the product from ethanol.

D.—Compound IV was converted to compound II by warming on a steam bath in acetic anhydride for a few minutes, cooling the solution, and filtering off the product.

2-Amino-7-chloro-3-hydroxy-5-phenyl-3*H*-1,4-benzodiazepine (IV). A.—To 3.0 g. of II suspended in 100 ml. of 50% alcohol was added with stirring 6 ml. of 4 *N* sodium hydroxide. When all of the solid had dissolved, the solution was acidified with acetic acid, diluted with water, and neutralized with sodium carbonate. The precipitated product was collected, washed with aqueous alcohol followed by acetonitrile, and recrystallized from isopropyl alcohol giving 1.5 g. of IV, m.p. 181–183°.

Anal. Calcd. for $C_{15}H_{12}ClN_3O$: C, 63.06; H, 4.24; N, 14.71; Cl, 12.41. Found: C, 63.45; H, 4.39; N, 15.00; Cl, 12.40.

(6) The melting points are uncorrected.

B.—To a suspension of 1.0 g. of lithium aluminum hydride in 75 ml. of ether was added with stirring 0.9 g. of VI. After 0.5 hr. the reaction mixture was cautiously treated with water to decompose the excess hydride, and the ether was filtered from the solids. Evaporation of the ether followed by several recrystallizations of the residue from cyclohexane and benzene gave IV, m.p. 181–183°.

7-Chloro-3-hydroxy-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepine (XIII), m.p. 202–204°, was prepared according to procedure A for IV from either XI or XII.

Anal. Calcd. for $C_{16}H_{14}ClN_3O$: C, 64.11; H, 4.71; N, 14.02; Cl, 11.83. Found: C, 64.26; H, 4.71; N, 14.26; Cl, 11.50.

3-Acetoxy-7-chloro-2-N-methylacetamido-5-phenyl-3*H*-1,4-benzodiazepine (XII).—Ten grams of X was heated in 250 ml. of acetic anhydride on the steam bath for 15 min., the solvent was removed *in vacuo*, and the residue was recrystallized from alcohol affording 3.1 g. of XII, m.p. 150–151°.

Anal. Calcd. for $C_{20}H_{18}ClN_3O_3$: C, 62.58; H, 4.72; N, 10.94; Cl, 9.23. Found: C, 62.21; H, 4.65; N, 10.67; Cl, 9.20.

3-Acetoxy-7-chloro-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepine (XI).—One and nine-tenths grams of X was heated in 40 ml. of acetic anhydride on the steam bath for 5 min., the solvent was removed *in vacuo*, and the residue was recrystallized from ethanol yielding 0.7 g. of XI, m.p. 200–202°.

Anal. Calcd. for $C_{18}H_{16}ClN_3O_2$: C, 63.25; H, 4.72; N, 12.29; Cl, 10.37. Found: C, 63.17; H, 4.78; N, 12.22; Cl, 10.21.

3-Acetoxy-7-chloro-1,3-dihydro-5-phenyl-2*H*-1-4-benzodiazepin-2-one (III).—A suspension of 2.0 g. of either II or XII in 50 ml. of alcohol containing 1 equivalent of hydrogen chloride was stirred until all of the solid dissolved. Upon dilution with an equal volume of water, a solid precipitated that was collected and recrystallized from ethanol to give white crystals of III, m.p. 241–243°.[2]

6-Chloro-4-phenylquinazoline-2-carboxylic acid (VII). A.—To a suspension of 2.0 g. of VI in 20 ml. of ethanol and 40 ml. of water was added with stirring 10 ml. of 4 *N* sodium hydroxide. The mixture was warmed to 40–50°. After 5 min. the mixture was filtered from undissolved matter, acidified with acetic acid, and the precipitated product was collected. Recrystallization from toluene gave 1.0 g. of VII, m.p. 215–216° (effervescent).

Anal. Calcd. for $C_{15}H_9ClN_2O_2$: C, 63.26; H, 3.19; N, 9.84; Cl, 12.46. Found: C, 63.28; H, 3.19; N, 9.84; Cl, 12.54.

B.—6-Chloro-3,4-dihydro-4-phenylquinazoline-2-carboxylic acid[2] (1 g.) was dissolved in 100 ml. of a dilute sodium hydroxide solution and a saturated solution of potassium permanganate was added until the color became permanent. The solution was filtered and acidified with acetic acid. Compound VII, m.p. 215–216° (effervescent), resulted.

2-Carbethoxy-6-chloro-4-phenylquinazoline (VIIa). A.—A mixture of 2.0 g. of VI in 25 ml. of ethanol and 25 ml. of 6 *N* hydrochloric acid was heated under reflux for 1 hr. The reaction mixture was concentrated to half volume and cooled, and the resultant precipitate was separated. The base was obtained by dissolving the precipitate in alcohol and adding an aqueous solution of triethylamine to give 1.0 g. of VIIa, m.p. 175–177°.

Anal. Calcd. for $C_{17}H_{12}ClN_2O_2$: C, 65.30; H, 4.19. Found: C, 65.39; H, 4.02.

B.—Compound VIIa also was prepared by esterification of VII, using thionyl chloride followed by ethanol.

6-Chloro-4-phenylquinazoline-2-carboxamide (IX). A.—A solution of 1.0 g. of VII in 10 ml. of thionyl chloride was heated under reflux for 1 hr. and then evaporated to dryness *in vacuo*. The residue was treated with alcoholic ammonia, and the product was collected and recrystallized from ethanol to give white crystals of IX, m.p. 264–266°.

Anal. Calcd. for $C_{15}H_{10}ClN_3O$: C, 63.49; H, 3.56; N, 14.85; Cl, 12.52. Found: C, 63.66; H, 3.65; N, 15.10; Cl, 12.60.

B.—A suspension of 1.0 g. of VIII in 30 ml. of 50% alcohol was treated with 1 equivalent of 1 *N* sodium hydroxide at room temperature. The resultant solution was acidified with acetic acid, and the precipitate was collected and recrystallized from alcohol to give IX, m.p. 264–266°.

Acknowledgment.—We wish to thank Dr. Gordon Ellis and his associates for the microanalyses and Mr. Bruce Hofmann for helpful discussions of the spectra.