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# Heterocycles. V.[1] Syntheses and Structures of 7-Chloro-2-hydrazino-5-phenyl-3*H*-1,4-benzodiazepines and Some Isomeric 1,4,5-Benzotriazocines[2]

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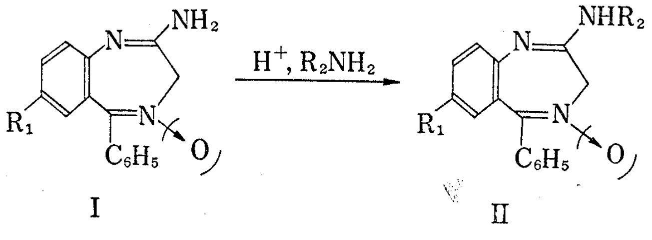
2-Hydrazino-1,4-benzodiazepine derivatives, III and X, were synthesized from the corresponding 2-amino derivatives Ia and Ib, respectively. It was found, on the other hand, that the reaction of a 2-chloromethylquinazoline 3-oxide (XIII) with hydrazine did not form X but gave a 2-hydroxyamino-1,4,5-benzotriazocine (XIV), which, after hydrogenation over Raney nickel, afforded its deoxygenated compound (XV). The structures of these diazepines and the isomeric triazocines were determined on the basis of chemical and physico-chemical behavior.

Novel tricyclic compounds, *s*-triazolo[4,3-*a*][1,4]benzodiazepines IX and XII were also prepared.

Our interest in the reactivity of the amidine moiety of 2-amino-1,4-benzodiazepines (I)[4] led us to the finding that the 2-position of I is susceptible to nucleophilic attack, as exemplified by their facile conversion to substituted 2-amino derivatives (II) by reaction with primary amines and hydroxylamines.[1] This paper deals with another application of the substitution reaction with hydrazine and the structure elucidation of the product. Some 1,4,5-benzotriazocines derived from a 2-chloromethylquinazoline 3-oxide are also described.

We found that 2-amino-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine (Ia) was easily converted into the corresponding 2-hydrazino-1,4-benzodiazepine (III) by reaction with hydrazine hydrate in methanol in the presence of an acid catalyst at room temperature. III gave a positive ninhydrin test (yellowish brown) and formed an isopropylidene derivative (IV) when recrystallized from acetone. III is somewhat unstable and formed, in boiling methanol, a bis-type compound (V) which is also isolated as a by-product in the reaction of Ia with hydrazine. Compound V has a molecular ion peak at *m/e* 536 in the mass spectrum. Both III and V gave the known 1,4-benzodiazepin-2-one (VI) on treatment with methanolic hydrogen chloride, while III regenerated Ia on heating with Raney nickel in methanol. Compound III was also prepared from both 1,4-benzodiazepine-2-thione (VII)[5] and its S-methyl derivative (VIII)[5] by the reaction with hydrazine hydrate.



$R_1$=H, Cl, $NO_2$
$R_2$=alkyl, substd. alkyl, OH, $OCH_3$, $OCH_2C_6H_5$

Chart 1

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[1] Part IV: K. Meguro, H. Natsugari, H. Tawada, and Y. Kuwada, *Chem. Pharm. Bull.* (Tokyo), **21**, 2366 (1973).

[2] This work has previously been communicated: K. Meguro and Y. Kuwada, *Tetrahedron Letters*, **1970**, 4039.

[3] Location: *Juso Higashiyodogawa-ku, Osaka, Japan.*

[4] K. Meguro, H. Tawada, and Y. Kuwada, *Yakugaku Zasshi*, **93**, 1253 (1972).

[5] G.A. Archer and L.H. Sternbach, *J. Org. Chem.*, **29**, 231 (1964).

Compound III was easily cyclized by treatment with ethyl orthoformate in ethanol in the presence of sulfuric acid at room temperature to an *s*-triazolo[4,3-*a*][1,4]benzodiazepine (IX) possessing a novel tricyclic ring system.

Similarly, starting with 2-amino-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide (Ib),[6] compounds X, XI and XII were obtained. Deoxygenation of XII with phosphorus trichloride or by catalytic hydrogenation over Raney nickel gave IX. Compound XII could also be obtained by oxidation of IX using *m*-chloroperbenzoic acid.

The structure of 2-hydrazino-1,4-benzodiazepines, III and X, is clearly supported by these chemical reactions and the spectral data of their derivatives. The structure was further confirmed by X-ray analysis[7] of IX.

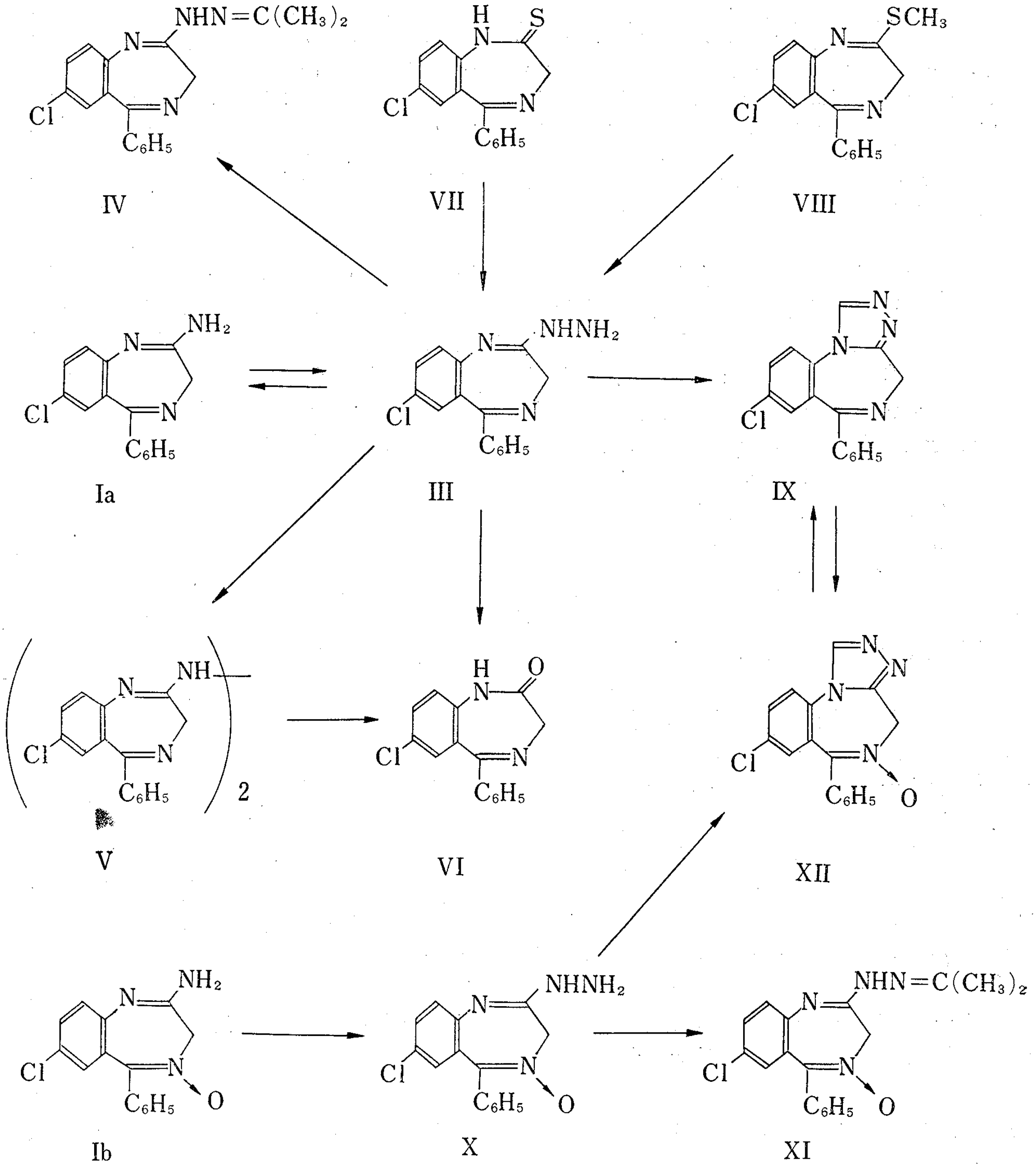

Chart 2

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[6] L.H. Sternbach and E. Reeder, *J. Org. Chem.*, **26, 1111 (1961).**

[7] K. Kamiya, Y. Wada, and M. Nishikawa, *Chem. Pharm. Bull.* (Tokyo), **21**, 1520 (1973).

Derieg, *et al.*[8] stated that the treatment of 6-chloro-2-chloromethyl-4-phenylquinazoline 3-oxide (XIII) with anhydrous hydrazine followed by hydrogenation over Raney nickel gave 7-chloro-2-hydrazino-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide (X) and its deoxygenated compound (III), respectively. However, the melting points they described for these products differ from those we obtained for X and III by our synthetic routes (Chart 2). We therefore repeated their experiments and obtained, instead, a hydroxyamino-1,4,5-benzotriazocine (XIV) and its deoxygenated compound (XV). We found that the same compound (XIV) could be synthesized more easily by the reaction of XIII with hydrazine hydrate in boiling methanol than with anhydrous hydrazine at room temperature as described by Derieg, *et al.*[8] Acetylation of XIV gave XVI, which, after saponification, afforded its monoacetyl derivative (XVII). Treatment of XIV with acetyl chloride in N,N-dimethylformamide gave XVIII. The melting points of the triazocines (XIV—XVIII) were in agreement with those reported[8] for the alleged diazepines.

Compounds XIV and XV were not colored by ninhydrin reagent and did not form isopropylidene derivatives. The oximes XIV and XVII gave positive ferric chloride and ammonium thiocyanate-ferric nitrate[9] tests, whereas XV, XVI and XVIII were negative to these reagents. The infrared (IR) spectrum of XVI showed bands at 1770 $cm^{-1}$ (suggesting the presence of an acetoxyl) and at 1666 $cm^{-1}$ (amide carbonyl). The band at 1770 $cm^{-1}$ was absent in the IR spectrum of XVII.

As shown in Fig. 1, the nuclear magnetic resonance (NMR) spectrum of XIV at 100 MHz in deuterated dimethyl sulfoxide showed the presence of an ABX coupling system attributable to the -$CH_2NH$- grouping. On addition of deuterium oxide or by irradiation of the NH proton (which appeared as a triplet at $\delta=7.86$, $J=7.0$ Hz), the pair of unresolved quartets due to the methylene collapsed into a pair of doublets ($\delta=3.39$ and $3.84$, $J=15.0$ Hz). On irradiation of the methylene protons, the NH signal collapsed to a singlet. Other NH or OH protons appeared at $\delta=8.59$ and $9.70$ as sharp singlets. The same coupling system was observed with XV but not with XVI and XVII.

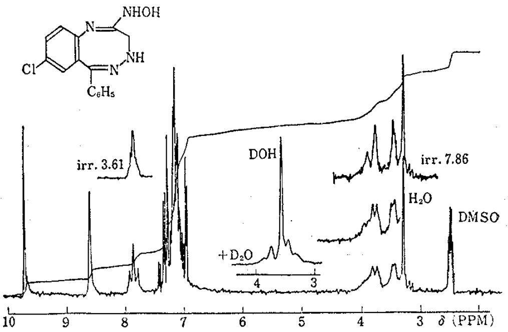

Fig. 1. The 100 MHz NMR Spectrum of XIV in DMSO-$d_6$

The above-mentioned chemical and physicochemical data indicate that XIV is not a diazepine as proposed by Derieg, *et al.*[8] but rather the isomeric cyclic amidoxime having an eight-membered 1,4,5-benzotriazocine ring. This was eventually confirmed by X-ray analysis[7] of compound XVI.

The NMR spectrum of compound XVIII showed the presence of three methyl groups but no signal attributable to methylene protons, suggesting that this compound is significantly different structurally from XIV-XVII. Although a rearrangement similar to that of α-tetralone oxime to 2-methyl-3′,4′-dihydro-naphtho-1′,2′:4,5-oxazole with acetic anhydride and hydrogen chloride[10] seemed plausible, there was no chemical evidence for the structure XVIII. The structure of XVIII, ultimately, was determined by X-ray crystallographic analysis.[7]

The reactions from XIII are, therefore, as depicted in Chart 3. Application of this reaction to a 2-(1-bromoethyl)quinazoline 3-oxide (XIX)[6] afforded the C-3 methyl analog (XX).

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[8] M.E. Derieg, R.I. Fryer, and L.H. Sternbach, *J. Chem. Soc.* (*C*), **1968**, **1103**.

[9] K.R. Manolov, *Fresenius, Z. Anal. Chem.*, 234, 37 (1961).

[10] N.N. Vorozhtsov and V.A. Koptiug, *J. Gen. Chem. USSR*, **28**, 1697 (1958).

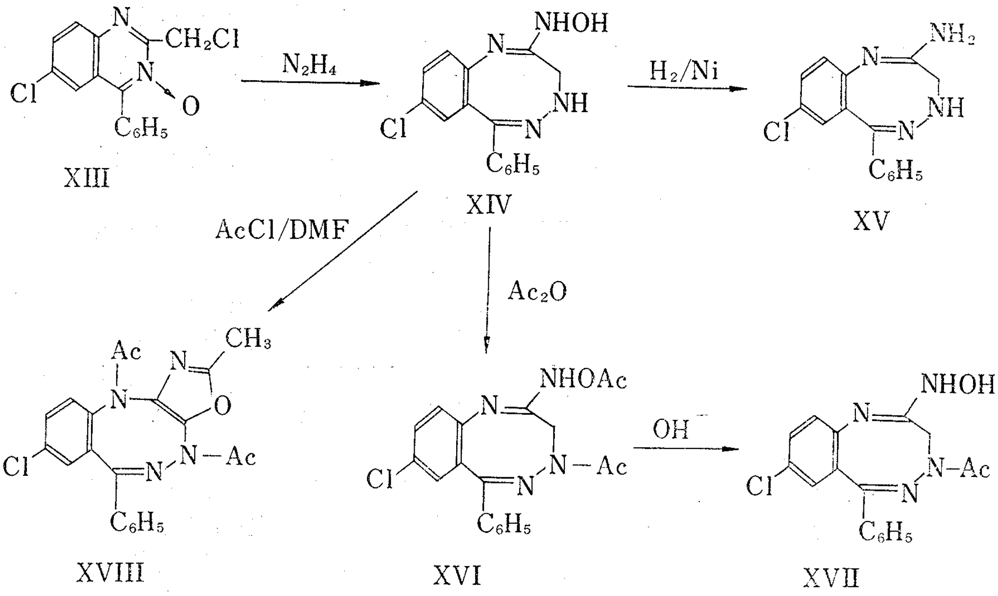
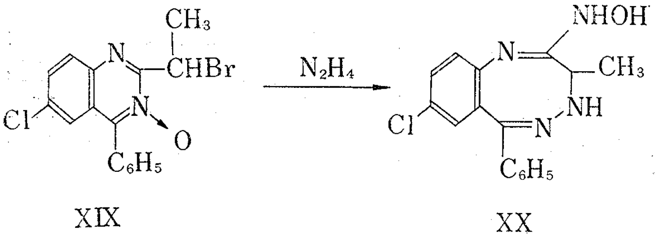


Chart 3



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The formation of XIV and XX suggests that ring opening of the quinazoline ring occurred at the N-3: C-4 bond, before or after the substitution of the halogeno function with hydrazine. A similar ring expansion accompanied by the ring opening of the quinazoline ring was recently reported by Giraldi, *et al.*[11] in the formation of a 2-hydroxyamino-4,1,5-benzoxadiazocine on treatment of XIII with hydroxylamine.

The 1,4-benzodiazepine derivatives reported in this paper showed depressant activity on the central nervous system but the triazocines did not. Especially strong activity was noted for 8-chloro-6-phenyl-4*H*-*s*-triazolo[4,3-*a*][1,4]benzodiazepine (IX)[12] as has been reported by Nakajima, *et al.*[13] in the Biological Research Laboratories of this Division.

## Experimental

All melting points were determined in open capillary tubes and are uncorrected. IR spectra were measured on a Hitachi EPI-S2 or on a Hitachi 215 spectrophotometer, ultraviolet (UV) spectra on a Perkin-Elmer 450 spectrophotometer, NMR spectra on a Varian A-60 (60 MHz) or on a Varian H-100 (100 MHz) spectrometer using tetramethylsilane as an internal standard, and mass spectra on a Hitachi RMU-6D double focussing mass spectrometer with a direct sample inlet system. The following abbreviations are used; sh=shoulder, s=singlet, d=doublet, t=triplet, m=multiplet, dd=doublet of doublet. Removal of solvents were performed on a rotary evaporator under water aspirator pressure. All solvents used in extractions were dried over sodium sulfate.

**7-Chloro-2-hydrazino-5-phenyl-3*H*-1,4-benzodiazepine (III)**——From Ia: a) To a stirred suspension of the crude dihydrochloride[4] (3.4 g) of 2-amino-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine (Ia) in MeOH (60 ml) was added dropwise 80% hydrazine hydrate (2.5 ml) at below 10°. While stirring was continued at 5—10°, the free base of Ia precipitated and was dissolved after about 1 hr. After 1.5 hr the solution was poured into ice water (200 ml) and extracted with $CHCl_3$ (100 ml × 2). The extract was washed with $H_2O$,

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[11] P.N. Giraldi, A. Fojanesi, G.P. Tosolini, E. Dradi, and W. Logemann, *J. Heterocyclic Chem.*, 7, 1429 (1970).

[12] This compound is also referred to as D-40TA (see ref. 13).

[13] R. Nakajima, C. Hattori, and Y. Nagawa, *Japan. J. Pharmacol.*, 21, 489 (1971); R. Nakajima, Y. Take, R. Moriya, Y. Saji, T. Yui, and Y. Nagawa, *ibid.*, 21, 497 (1971).

dried and evaporated. The residue was crystallized from benzene to yield colorless crystals (2.2 g, 79%), mp 170— (browning), 204—205° (decomp.). Recrystallization from $CH_2Cl_2$–benzene gave an analytical sample as colorless prisms, mp 170— (browning), 202—204° (decomp.).[14] *Anal.* Calcd. for $C_{15}H_{13}N_4Cl$: C, 63.27; H, 4.60; N, 19.68. Found: C, 63.43; H, 4.48; N, 19.27. Ninhydrin (yellowish brown). UV $\lambda_{\max}^{\text{iso-PrOH}}$nm ($\varepsilon$): 250 sh (22400). NMR ($CDCl_3$) $\delta$: 4.18 (2H, s, $-CH_2-$), 4.94 (3H, b, $NHNH_2$). This compound was sometimes obtained as yellowish fine prisms containing 1/3 mole eq. of $CH_2Cl_2$ of crystallization, mp 176 (browning)—195° (decomp.). *Anal.* Calcd. for $C_{15}H_{13}N_4Cl \cdot 1/3CH_2Cl_2$: C, 58.82; H, 4.40; N, 17.90. C, 58.75; H, 4.29; N, 17.98.

Isopropylidene Derivative (IV): Recrystallization of the crude III from acetone gave IV as colorless needles of mp 184.5—185.5°. *Anal.* Calcd. for $C_{18}H_{17}N_4Cl$: C, 66.56; H, 5.28; N, 17.25. Found: C, 66.49; H, 5.28; N, 17.03. UV $\lambda_{\max}^{\text{MeOH}}$ nm ($\varepsilon$): 260 (29300). NMR ($CDCl_3$) $\delta$: 2.04 ,2.07 (each 3H, s, $(CH_3)_2$), 4.49 (2H, s, $-CH_2-$).

b) To a stirred mixture of Ia (8.1 g), MeOH (150 ml) and AcOH (1.8 ml) was added dropwise hydrazine hydrate (4.5 ml) at room temperature. The mixture was stirred for 45 min and the product (III) was isolated in the manner described in a). Yield, 6.1 g (72%).

From VII: A mixture of 7-chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepine-2-thione (VII, 287 mg), EtOH (15 ml) and hydrazine hydrate (0.15 ml) was stirred at room temperature for 20 min, poured into ice water and extracted with $CHCl_3$. The product (232 mg, 81.4%) obtained from the extract was recrystallized from $CH_2Cl_2$–benzene to yield colorless crystals, mp 203—205° (decomp.). This product was found to be identical with the sample prepared from Ia by IR and NMR comparison.

From VIII: A solution of 7-chloro-2-methylmercapto-5-phenyl-3*H*-1,4-benzodiazepine (VIII, 1 g) and 80% hydrazine hydrate (3 ml) in EtOH (35 ml) was allowed to stand at room temperature for 3 days. The solution was concentrated and extracted with $CH_2Cl_2$. The extract was washed with $H_2O$, dried, and evaporated to give colorless crystals (600 mg, 63%), mp 218—220°. This product was contaminated with a considerable amount of a bis-type compound (V)[14b] and was characterized as the isopropylidene derivative (IV) by its mp (184—185°) and by the identity of its IR spectrum with IV prepared by an alternate route (*vide supra*).

**N,N′-Bis(7-chloro-5-phenyl-3*H*-1,4-benzodiazepin-2-yl)hydrazine (V)**——A solution of III (284 mg) in MeOH (20 ml) was refluxed for 4 hr and the precipitate was filtered off to afford V (70 mg, 26%). Recrystallization from $CHCl_3$–*n*-hexane gave colorless needles of mp 253—254°. *Anal.* Calcd. for $C_{30}H_{22}N_6Cl_2$: C, 67.04; H, 4.12; N, 15.63. Found: C, 67.04; H, 3.97; N, 15.69. Mass Spectrum *m/e*: 536 ($M^+$).

This product was often isolated as a by-product from the mother liquors of the reaction of Ia→III in *ca.* 5—7% yield.

**7-Chloro-2,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one (VI)**——From III: A solution of III (142 mg) in a mixture of MeOH (5 ml) and 10% methanolic hydrogen chloride (1 ml) was refluxed for 2 hr. The solvent was evaporated and the residue was partitioned between $CH_2Cl_2$ and saturated aq. $NaHCO_3$. The organic phase was separated, washed with $H_2O$ and dried. After removal of the solvent, the residue was recrystallized from acetone to give colorless plates (55 mg, 40%), mp 212—213°, which was identical with an authentic sample of VI by IR comparison.

From V: When V was treated under the same condition as above, VI was obtained in 33% yield as colorless plates of mp 213—214°.

**Reduction of III with Raney Nickel**——A mixture of III (285 mg), MeOH (7 ml) and Raney Ni (1.2 g, wet) was refluxed for 1 hr, after which the catalyst was removed by filtration. The filtrate was concentrated and the precipitate was collected and recrystallized from MeOH to afford colorless prisms (155 mg, 57%), mp 233—235° (decomp.). The IR spectrum of this compound was identical with that of authentic Ia.

**7-Chloro-2-hydrazino-5-phenyl-3*H*-1,4-benzodiazepine 4-Oxide (X)**——To a suspension of 2-amino-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide (Ib, 14.3 g) in MeOH (400 ml) were added hydrazine hydrate (12.5 ml) and saturated methanolic hydrogen chloride (10 ml). The mixture was then heated on a boiling water bath until a clear solution was obtained (*ca.* 10 min). The solution was concentrated to about the half volume and poured into $H_2O$ (500 ml). The product was taken up with $CHCl_3$ (200 ml × 2) and the extract was washed with $H_2O$, dried and concentrated. Addition of ether to the residue gave pale yellow crystalline powder (14.0 g, 93.5%), mp 262—263° (decomp.), which was positive to ninhydrin reagent (yellowish brown). *Anal.* Calcd. for $C_{15}H_{13}ON_4Cl$: C, 59.90; H, 4.36; N, 18.63. Found: C, 60.05; H, 4.13; N, 18.41. UV $\lambda_{\max}^{\text{iso-PrOH}}$nm ($\varepsilon$): 244 (24800), 267 (23600). NMR ($CDCl_3$) $\delta$: 4.51 (2H, s, $-CH_2-$), *ca.* 5.60 (3H, very b, $NH-NH_2$).

Isopropylidene Derivative (XI): A solution of X (300 mg) in acetone (5 ml) was refluxed for 10 min and a small amount of insoluble matter was filtered off. The filtrate was concentrated and the precipitated

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14) *a*) Very slow heating in the measurement of the melting point of III causes a rise in its value, because of the gradual formation of a bis-type compound (V); *b*) Contamination of V also tends to increase the mp value; *c*) Recently mp 217.5—219° was reported for III by J.B. Hester, Jr., D.J. Duchamp, and C.G. Chidester, *Tetrahedron Letters*, **1971**, 1609.

product (XI) was filtered off to yield colorless needles, mp 223—224°. *Anal.* Calcd. for $C_{18}H_{17}ON_4Cl$: C, 63.43; H, 5.03; N, 16.44. Found: C, 63.44; H, 4.84; N, 16.41. UV $\lambda_{max}^{MeOH}$ nm ($\varepsilon$): 246 (26300), 280 (29800). NMR ($CDCl_3$) $\delta$: 2.06, 2.11 (each 3H, s, $(CH_3)_2$), 4.76 (2H, s, $-CH_2-$).

**8-Chloro-6-phenyl-4*H*-s-triazolo[4,3-*a*][1,4]benzodiazepine (IX)**——From III: To a stirred mixture of III (5.7 g), ethyl orthoformate (12 g) and EtOH (100 ml) was added dropwise conc. $H_2SO_4$ (2.2 ml). After stirring was continued at room temperature for 30 min (color of the solution changed red to yellow), the mixture was diluted with aq. $NaHCO_3$ and concentrated. The precipitate was collected, washed with $H_2O$ and ether, and recrystallized from acetone–*n*-hexane to yield colorless plates (5.1 g, 86%), mp 226—227°. *Anal.* Calcd. for $C_{16}H_{11}N_4Cl$: C, 65.20; H, 3.76; N, 19.01. Found: C, 65.30; H, 3.48; N, 19.03. UV $\lambda_{max}^{MeOH}$ nm ($\varepsilon$): 223 (46300), 247 sh (17000); $\lambda_{max}^{2N\ HCl}$ nm ($\varepsilon$): 269 (10500). NMR ($CDCl_3$) $\delta$: 4.90 (2H, b, $-CH_2-$), 8.61 (1H, s, C–1 H). Mass Spectrum *m/e*: 294 ($M^+$).

From XII: a) A mixture of XII (310 mg), $CHCl_3$ (20 ml) and $PCl_3$ (0.53 ml) was refluxed for 1 hr and concentrated to dryness. The residue was partitioned between saturated aq. $NaHCO_3$ and $CHCl_3$. The organic phase was separated, washed with $H_2O$, dried ,and evaporated. The residue was treated with ether to give colorless crystals (250 mg, 85%), mp 219—221°. Recrystallization from AcOEt afforded colorless plates of mp 223—224°. This product exhibited an identical IR spectrum with that for IX prepared from III.

b) XII (310 mg) was hydrogenated over Raney Ni (1 g, wet) in a mixture of EtOH (10 ml) and MeOH (20 ml) at room temperature and atmospheric pressure for 5 hr (27.5 ml of hydrogen was consumed). After filtration, the filtrate was concentrated to dryness and the residue crystallized from AcOEt as colorless plates (140 mg, 47.5%), mp 222—223°. The IR spectrum of this crystals was identical with that for IX.

**8-Chloro-6-phenyl-4*H*-s-triazolo[4,3-*a*][1,4]benzodiazepine 5-Oxide (XII)**——From X: To a stirred mixture of X (3 g), ethyl orthoformate (7.4 g) and EtOH (100 ml) was added dropwise conc. $H_2SO_4$ (1.1 ml) and the resulting solution was stirred at room temperature for 30 min. The solution was then concentrated and made alkaline with aq. $NaHCO_3$. The crystals which precipitated were collected, washed with $H_2O$ and ether, and dried to yield XII (2.9 g, 94%), mp 254—257° (decomp.). Recrystallization from a mixture of $CHCl_3$ and MeOH (1: 1, v/v) gave colorless needles of mp 267—268° (decomp.). *Anal.* Calcd. for $C_{16}H_{11}ON_4Cl$: C, 61.74; H, 3.57; N, 18.03. Found: C, 61.87; H, 3.26; N, 17.92. UV $\lambda_{max}^{MeOH}$ nm ($\varepsilon$): 230 (29800), 256 (17600), 310 (11600); $\lambda_{max}^{2N\ HCl}$ nm ($\varepsilon$): 233 (24400), 307 (10400). NMR (DMSO-$d_6$) $\delta$: 5.38 (2H, s, $-CH_2-$), 9.30 (1H, s, C-1 H). Mass Spectrum *m/e*: 310 ($M^+$).

From IX: To a stirred, cold (0—3°) solution of IX (590 mg) in $CH_2Cl_2$ (10 ml) was added dropwise a solution of *m*-chloroperbenzoic acid (380 mg) in $CH_2Cl_2$ (5 ml). The solution was then stored in a refrigerator at 4° for 72 hr. After the addition of 2N NaOH (5 ml), the mixture was stirred and the resulting precipitate was filtered off, washed with $H_2O$ and $CH_2Cl_2$ and dried to yield XII (244 mg). The organic phase of the filtrate was separated, washed with $H_2O$, dried and evaporated to leave a crystalline residue which was collected and washed with MeOH. The combined crystals (439 mg, 71%) was recrystallized from $CHCl_3$–MeOH to give colorless needles of mp 268—270° (decomp.). This product showed an identical IR spectrum with a sample prepared from X.

**8-Chloro-3,4-dihydro-2-hydroxyamino-6-phenyl-1,4,5-benzotriazocine (XIV)**——a) By the reaction of 6-chloro-2-chloromethyl-4-phenylquinozaline 3-oxide (XIII) with anhydrous hydrazine under the condition described by Derieg, *et al.*,[8] XIV was obtained in 10% yield (lit.[8] 35.6%) as colorless crystals of mp 232—235° (decomp.) [lit.[8] mp 235—238° (decomp.)]. Ninhydrin (—), $FeCl_3$ (+, deep green). *Anal.* Calcd. for $C_{15}H_{13}ON_4Cl$: C, 59.90; H, 4.36; N, 18.63. Found: C, 60.17; H, 4.18; N, 18.86. UV $\lambda_{max}^{iso\text{-}PrOH}$ nm ($\varepsilon$): 266 (23800). NMR: see Fig. 1.

b) The same compound (XIV) was synthesized by an improved method as follows; To a stirred suspension of XIII (6 g) in MeOH (200 ml) was added dropwise hydrazine hydrate (4 ml) over a period of 5 min under reflux. As the heating was continued, XIII dissolved and then colorless crystals precipitated. The product was collected after 30 min to yield XIV (3.4 g, 57%), mp 231—234° (decomp.). Recrystallization from DMF–$H_2O$ gave colorless needles, mp 233—235° (decomp.). The IR spectrum of this product was identical with XIV prepared in a).

**2-Amino-8-chloro-3,4-dihydro-6-phenyl-1,4,5-benzotriazocine (XV)**——Hydrogenation of XIV (2 g) over Raney Ni (2 g, wet) in MeOH (30 ml) gave XV in quantitative yield. Recrystallization from EtOH–petr. ether afforded colorless needles (1.5 g, 79%), mp 174—175° (lit.[8] mp 175—179°). Ninhydrin (—), $FeCl_3$ (—). *Anal.* Calcd. for $C_{15}H_{13}N_4Cl$: C, 63.27; H, 4.60; N, 19.68. Found: C, 63.56; H, 4.38; N, 19.49. UV $\lambda_{max}^{iso\text{-}PrOH}$ nm ($\varepsilon$): 263 (22300). NMR ($CDCl_3$, 100 MHz) $\delta$: 2.95 (1H, dd, $J=14.0$ Hz, 6.6 Hz, $-C\underline{H}(H)-$), 4.11 (1H, dd, $J=14.0$ Hz, 8.2 Hz, $-CH(\underline{H})-$), 4.71 (2H, b, $NH_2$), 6.58 (1H, unresolved t, NH).

**2-Acetoxyamino-4-acetyl-8-chloro-3,4-dihydro-6-phenyl-1,4,5-benzotriazocine (XVI)**——Acetylation of XIV (600 mg) with $Ac_2O$ (3 ml) in dry pyridine (6 ml) at room temperature overnight followed by recrystallization of the product from $CHCl_3$–*n*-hexane gave colorless plates (660 mg, 90%), mp 228—230°. Further recrystallization from MeOH afforded needles of mp 230—231° (lit.[8] mp 230—231.5°). $FeCl_3$ (—). *Anal.* Calcd. for $C_{19}H_{17}O_3N_4Cl$: C, 59.30; H, 4.45; N, 14.56. Found: C, 59.47; H, 4.30; N, 14.63. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1770 (ester), 1666 (amide). UV $\lambda_{max}^{MeOH}$ nm ($\varepsilon$): 253 (26200). NMR ($CDCl_3$) $\delta$: 2.14, 2.44 (each 3H, s, $-COCH_3$), 3.99, 5.53 (each 1H, d, $J=14.5$ Hz, $-CH_2-$), 7.67 (1H, s, NH).

**4-Acetyl-8-chloro-3,4-dihydro-2-hydroxyamino-6-phenyl-1,4,5-benzotriazocine (XVII)**——After alkaline hydrolysis of XVI (184 mg) the product was recrystallized from EtOH–$H_2O$ to give colorless needles (129 mg, 79%), mp 225—226° (lit.[8] mp 225—226°). $FeCl_3$ (+, deep green). *Anal.* Calcd. for $C_{17}H_{15}O_2N_4Cl$: C, 59.56; H, 4.41; N, 16.35. Found: C, 59.66; H, 4.38; N, 16.59. IR $\nu_{\max}^{\text{KBr}}$ $cm^{-1}$: 1658 (amide). UV $\lambda_{\max}^{\text{MeOH}}$ nm ($\varepsilon$): 259 (20700). NMR (DMSO-$d_6$, 100 MHz) $\delta$: 2.44 (3H, s, $-COCH_3$), 3.91, 5.36 (each 1H, d, $J=15.0$ Hz, $-CH_2-$), 8.02, 9.83 (each 1H, s, NHOH).

**8-Chloro-4,11-diacetyl-4,11-dihydro-2-methyl-6-phenyl-oxazolo[4,5-*b*][1,4,5]benzotriazocine (XVIII)**——On treatment of XIV (300 mg) with acetyl chloride (0.7 ml) in DMF (5 ml) followed by treatment in the usual manner gave crystals which were recrystallized from EtOH–petr. ether as pale yellow prisms (88 mg, 22%), mp 172—174° (lit.[8] mp 176—178°). *Anal.* Calcd. for $C_{21}H_{17}O_3N_4Cl$: C, 61.69; H, 4.19; N, 13.71. Found: C, 61.58; H, 4.11; N, 13.71. IR $\nu_{\max}^{\text{KBr}}$ $cm^{-1}$: 1695 (amide). UV $\lambda_{\max}^{\text{MeOH}}$ nm ($\varepsilon$): 254 (21400).

**8-Chloro-3,4-dihydro-2-hydroxyamino-3-methyl-6-phenyl-1.4,5-benzotriazocine (XX)**——To a stirred suspension of 2-(1-bromoethyl)-6-chloro-4-phenylquinazoline 3-oxide (XIX, 1.80 g) in MeOH (40 ml) was added dropwise 80% hydrazine hydrate (1.0 ml) and the mixture was refluxed for 30 min. After cooling, the precipitate was collected by filtration and washed with MeOH to give colorless crystals (750 mg, 48%), mp 203—205° (decomp.). Recrystallization from $CHCl_3$–MeOH afforded colorless needles of mp 212—214° (decomp.). *Anal.* Calcd. for $C_{16}H_{15}ON_4Cl$: C, 61.05; H, 4.77; N, 17.81. Found: C, 61.11; H, 4.83; N, 18.02. NMR (DMSO-$d_6$) $\delta$: 1.20 (3H, d, $J=5.6$ Hz, $C\underline{H}_3-CH\langle$), 4.31 (1H, m, $-NH-\underset{|}{C\underline{H}}-CH_3$), 7.51 (1H, b, $-N\underline{H}-CH\langle$), 8.58, 9.82 (each 1H, s, $-NHOH$).

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