kept at 45 °C for 22 h. Fine white crystals separated on cooling. The mixture was extracted with CH_2Cl_2. After the extracts were washed with water, dried, and evaporated, crystallization from CH_2Cl_2–ether gave 43 mg (68%) of **22**: mp 212–215 °C; λ_{max} (MeOH) 234 (ϵ 31 000), 280 (14 000), (sh)) nm; ν (KBr) 3315, 1730, 1700, 1680, 1660, 1630 cm^{-1}; δ ($CDCl_3$) 1.84 (s, 3), 2.22 (s, 3), 7.0–8.3 (m, 13), 9.2–9.5 (br s, 1); m/e(calcd) for $C_{21}H_{20}N_2O_4$ 364.121, m/e(found) 364–121.

Anal. Calcd for $C_{21}H_{20}N_2O_4$: C, 69.21; H, 5.53. Found: C, 69.29; H, 5.45.

Reaction of 16 in Ethanol. A solution of 25 mg of 1,3-diazepine **16** in 2 mL of absolute ethanol was allowed to stand for 2 weeks at 22 °C; the color changed from yellow to pale orange. The solution was evaporated and after traces of ethanol were codistilled with CCl_4, the ^1H NMR spectrum ($CDCl_3$) showed CH_3 signals for unreacted **16** at δ 1.77 and 2.32 and the following peaks due to **23**: δ 1.97 (t, J = 7 Hz, CH_3CH_2), 1.74 (s, ring CH_3), 2.22 ($COCH_3$), 2.70 (q, J = 7 Hz, CH_3CH_2O), 5.78 (m, NH), 6.44 (d, J = 3.2 Hz, C2-H). Deuterium exchange caused loss of the 5.78 peak and the peak at 6.44 became a singlet. The areas of the two sets of peaks were in ratio of ~1:1. After the analyte was redissolved in ethanol and the resulting solution allowed to stand for 6 weeks, the peaks due to **23** and **16** were in a ratio of about 8–9:1, and the CCH_3 peak of **22** was visible at δ 1.86.

Reaction of 16 with Base. To a solution of 100 mg of **16** in 2.5 mL of methanol was added 0.7 mL of aqueous 1.0 N NaOH. After 3 h at 25 °C the pale yellow solution was acidified with 2 N HCl and then neutralized with $NaHCO_3$. At neutral pH the amphoteric product crystallized as a white solid: 80 mg; mp 115–126 °C. This was identified by IR and ^1H NMR comparison as the methanol solvate of the 6-benzamido-3-hydroxypyridine **14b**. Recrystallization from $CHCl_3$–ether gave crystals: mp 214–217 °C; the mixture melting point with **14b** of mp 212 °C showed no depression.

Crystallographic Analysis of 22. The crystals of **22** were monoclinic, space group $P2_1/n$, with a = 18.838 (4) Å, b = 19.853 (5) Å, c = 10.580 (4) Å, β = 95.68 (3)°, and d_{calcd} = 1.229 g cm^{-3} for Z = 8 (M_r = 364.40 for $C_{21}H_{20}N_2O_4$). The intensity data were collected on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse-height discrimination). A crystal measuring approximately 0.10 × 0.12 × 0.4 mm was used for data collection; the data were not corrected for absorption (μ = 7.1 cm^{-1}). A total of 3735 reflections were measured for θ < 48°, of which 2769 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple-solution procedure[21] and was refined by full-matrix least squares. In the final refinement anisotropic thermal parameters were used for the heavier atoms and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations but their parameters were not refined. The final discrepancy indices are R = 0.048 and R_w = 0.051 for the 2769 observed reflections. The final difference map has no peaks greater than ±0.2 e A^{-3}.

Registry No. 9a, 40711-78-2; **9b**, 40711-79-3; **9c**, 40711-81-7; **9d**, 40711-80-6; **10b**, 17827-20-2; **11a**, 40711-83-9; **11b**, 65594-62-9; **11c**, 40711-84-0; **12a**, 40711-76-0; **13b**, 70321-02-7; **14a**, 10137-08-3; **14b**, 10137-10-7; **14c**, 70321-03-8; **14d**, 70321-04-9; **15a**, 70321-05-0; **15b**, 65594-63-0; **15c**, 70321-06-1; **16b**, 65594-64-1; **17**, 70321-07-2; **22**, 70321-09-4; **23**, 70321-10-7; **8**, 70321-01-6; **17** acetyl derivative, 70321-08-3.

Supplementary Material Available: Tables I–V containing final atomic parameters, anisotropic thermal parameters, bond lengths, bond angles, and torsion angles for **22** (6 pages). Ordering information is given on any masthead page.

(21) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr. Sect. A*, **1971**, *27*, 368.

Synthesis and Chemistry of *N*-Methyl-6-phenyl-4*H*-*s*-triazolo[4,3-*a*][1,4]benzodiazepinium Derivatives

Jackson B. Hester, Jr.,* Constance G. Chidester, and Jacob Szmuszkovicz

Research Laboratories, The Upjohn Company, Kalamazoo, Michigan 49001

Received March 5, 1979

8-Chloro-1-methyl-6-phenyl-4*H*-*s*-triazolo[4,3-*a*][1,4]benzodiazepine was alkylated at N-2 of the triazole ring with trimethyloxonium fluoroborate. Mild alkaline hydrolysis of this derivative cleaved the triazole system to give acetic acid 2-(7-chloro-5-phenyl-3*H*-1,4-benzodiazepin-2-yl)-1-methylhydrazide, the structure of which was confirmed by an independent synthesis. The synthesis of several 8-chloro-3-methyl-6-phenyl-4*H*-*s*-triazolo-[4,3-*a*][1,4]benzodiazepinium derivatives is also presented.

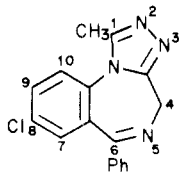
The discovery that the 6-phenyl-4*H*-*s*-triazolo[4,3-*a*]-[1,4]benzodiazepines[1,2] (viz., alprazolam, **4**; see Chart I) have useful anxiolytic activity[3] has generated an intense interest in the chemistry of this class of compounds. Early in the development of this series we became interested in the structural requirements for biological activity. In particular we wondered if the seven-membered ring was required or if the biological activity might be retained if the ring were opened between N-5 and C-6 to give an amino benzophenone. From independent synthetic studies we had found that the primary amino ketone was unstable relative to the cyclic structure.[4] We therefore decided to alkylate this nitrogen (N-5 of **1**) and thus stabilize the ring-opened form. Since we had previously found that alkylation of **2** with trimethyloxonium fluoroborate occurred exclusively at N-5 to give, after aqueous workup, the ring-opened product,[5] we chose these conditions for the present study. In the event, however, alkylation of **1** with the Meerwein reagent occurred on the triazole ring rather than on the azepine nitrogen (N-5).[6] This paper describes these results.

Alkylation of **1** with trimethyloxonium fluoroborate followed by hydrolysis of the product with aqueous potassium carbonate at ambient temperature gave a ring-

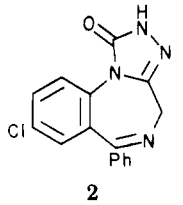
(1) J. B. Hester, Jr., A. D. Rudzik, and B. V. Kamdar, *J. Med. Chem.*, **14**, 1078 (1971).
(2) K. Meguro, H. Tawada, H. Miyano, Y. Sato, and Y. K. Uwada, *Chem. Pharm. Bull.*, **21** 2382 (1973).
(3) T. M. Itil, N. Polvan, S. Egilmez, B. Saletu, and J. Marasa, *Curr. Ther. Res. Clin. Exp.*, **15**, 603 (1973).
(4) J. B. Hester, Jr., U.S. Patent 3 709 898 (1973).
(5) J. B. Hester, Jr., and P. F. VonVoigtlander, *J. Med. Chem.*, in press.
(6) The successful preparation of the ring-opened compounds is described in M. Gall, J. B. Hester, Jr., A. D. Rudzik, and R. A. Lahti, *J. Med. Chem.*, **19**, 1057 (1976).

0022-3263/79/1944-2688$01.00/0

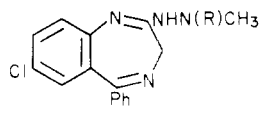
Chart I



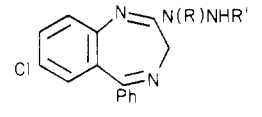
1



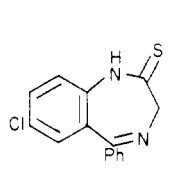
2



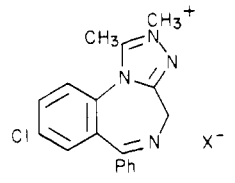
3, R = H
4, R = C(=O)CH$_3$



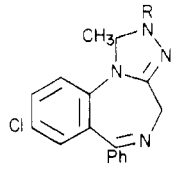
5, R = R' = H
6, R = H; R' = C(=O)CH$_3$
7, R = CH$_3$; R' = H
8, R = CH$_3$; R' = C(=O)CH$_3$



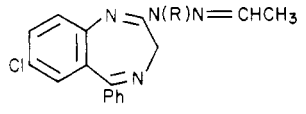
9



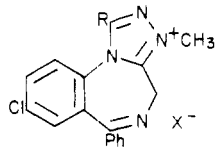
10



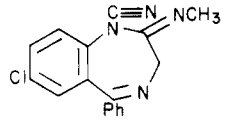
11, R = CH$_3$
12, R = H



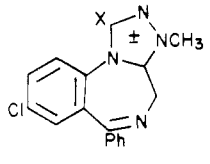
13, R = H
14, R = CH$_3$



15, R = CH$_3$
16, R = H
17, R = NH$_2$



18



19, X = O
20, X = S
21, X = NC(=O)CH$_3$

opened derivative (4) which was isomeric with the expected benzophenone but which lacked the expected carbonyl band at 1665 cm^{-1} in the infrared spectrum. An amide carbonyl band at 1625 cm^{-1} was present, however. In addition, the NMR signal for the C-1 methyl group which had originally been at δ 2.62 in 1 was now found at δ 1.95, a location compatible with that of the C-methyl of an acetamide. We thus proposed that alkylation of 1 had occurred on one of the triazole ring nitrogens and that subsequent hydrolysis had proceeded by attack of hydroxide anion at C-1 to open the triazole ring and give an acetamide (viz., 4 or 8). The site of alkylation was, however, ambiguous and the exact nature of the proposed hydrolysis product had to be confirmed. Reaction of the thione 9 with methylhydrazine gave a mixture of 3 and 7 from which 7 could be isolated either by direct crystallization or by silica gel chromatography of the crude reaction mixture. Compound 3, however, could not be eluted from the column nor could it be isolated by crystallizing the crude product. Subsequent reactions on this compound (3), therefore, had to be carried out on the crude mixture. Thus the reaction of the mixture with acetic anhydride in THF, a reaction which gave exclusively the terminal acylation product (6) from 5, resulted in a mixture of two isomeric acylation products one of which was identical with the product (4) obtained from 1. The second product (8) was also obtained as the exclusive acylation product from pure 7. The mass spectrum of 4 exhibited a relatively intense ion at m/e 269 which was not present in the spectrum of 8. This ion corresponds to the loss of $CH_2{=}NC(=O)CH_3$ from the molecular ion, a fragmentation that would result from a McLafferty rearrangement.[7] Compound 8 on the other hand had an intense ion at m/e 282 which corresponds to the loss of $CH_3C(=O)NH$ from the molecular ion; this ion was not present in the spectrum of 4. These results support the assigned structures of 4 and 8 and, since 4 was obtained by alkylating 1, they support structure 10 for the initial alkylation product. This material (10, X = BF_4) was isolated as a solid from the crude alkylation mixture prior to alkaline hydrolysis; it was characterized as the bromide (10, X = Br) which was obtained by exchange of the BF_4 ion with potassium bromide in aqueous ethanol. The physical properties of this material were in complete agreement with those expected for the assigned structure. Reduction of 10 (X = BF_4) with sodium borohydride gave 11, a yellow solid which was sensitive to air oxidation. This same compound (11) was obtained when the crude mixture of 3 and 7 was treated with acetaldehyde. Compounds 4 and 14 were also obtained from the latter reaction. Compound 11 is undoubtedly the initial cyclodehydration product obtained from the reaction of 3 with acetaldehyde. We suspected that 4 might be a secondary product obtained from 11 by air oxidation. This was substantiated by the finding that a solution of 11 in wet ethyl acetate–chloroform did in fact react with air to give 4 in 38% yield. In this regard it should also be noted that air oxidation of 13 gave 1; this reaction may proceed via oxidation of a cyclic intermediate such as 12.[8]

Compound 14 is the product expected from the reaction of 7 with acetaldehyde. It was in fact the only product obtained from the reaction of pure 7 with acetaldehyde. Identification of this material, however, was confounded by the fact that a signal corresponding to the C-3 methylene protons could not be detected in the NMR spectrum.[9a] The ultimate resolution of this problem was obtained by X-ray crystallography which confirmed structure 14. Details of this analysis are in the Experimental Section.[9b]

(7) F. W. McLafferty, "Interpretation of Mass Spectra", W. A. Benjamin, New York, N.Y., 1966, p 123.

(8) (a) Oxidation of 13 with activated manganese dioxide or diethyl azodicarboxylate has also been reported to give 1.[20] (b) Other members of this series have also been prepared by this method: J. B. Hester, Jr., and J. Szmuszkovicz, Deutsche Offenlegungsschrift 2242938 to The Upjohn Co. (March 15, 1973).

(9) (a) A question by both reviewers regarding the reason for this phenomenon prompted us to reinvestigate the NMR spectrum of this compound (14). At ambient temperature [$(CD_3)_2SO$, 100 MHz] the C-4 methylene protons were observed as two very broad singlets centered at about δ 6.0 and 3.2; at 80 °C both protons were found in a broad singlet centered at about δ 4.6. Apparently in the original spectra run at ambient temperature, the signals were too broad to be detected by the 60-MHz instrument. The integrity of the C-4 methylene was also demonstrated by the ^{13}C NMR spectrum [$CDCl_3$, 20 MHz] which had a peak for this carbon at δ 47.98 from Me_4Si. We are indebted to Mr. T. A. Scahill of our Physical and Analytical Chemistry Department for carrying out these studies. (b) Tables of final parameters and full details of the crystal structure analysis will be published elsewhere.

The 3-methyl isomer (**15**, X = $C_7H_7SO_3$) of **10** was prepared by the reaction of **7** with triethyl orthoacetate and *p*-toluenesulfonic acid.[10] Conversion of the *p*-toluenesulfonate salt to the corresponding chloride (**15**, X = Cl) was accomplished by the use of an anion-exchange column. As would be predicted[11] based on the proximity of the quaternary nitrogen to the 1-position of the triazole ring, the NMR peak for the 1-methyl group of **10** (X = Br) was found at lower field (δ 3.28) than the corresponding peak (δ 2.87) of **15** (X = $C_7H_7SO_3$). An attempt to obtain a ring-cleavage product by the reaction of **15** (X = $C_7H_7SO_3$) with aqueous sodium hydroxide was unsuccessful. Preparation of the homologous 3-methyl derivative (**16**) was accomplished by the reaction of **7** with triethylorthoformate and sulfuric acid. It was converted to its chloride salt (**16**, X = Cl) by neutralizing a solution of **16** (X = HSO_4) in saturated sodium chloride with sodium bicarbonate and extracting the mixture with chloroform. When treated with aqueous sodium hydroxide this material (**16**, X = HSO_4) gave the triazole ring-cleavage product (**18**) by a reaction that is probably initiated by removal of the C-1 proton. An analogous reaction for benzisoxazoles has been described in detail.[12]

The availability of **7** made it possible to prepare several mesoionic[13] analogues of **1**. Thus condensation of **7** with phosgene in the presence of triethylamine gave the oxygen derivative **19**. A similar reaction with thiophosgene gave **20** while condensation of **7** with cyanogen bromide resulted in a salt (**17**, X = Br) which was converted to **17** (X = Cl) by means of an anion-exchange resin. When **17** (X = Cl) was acylated with acetic anhydride and triethylamine, the mesoionic derivative **21** was obtained. The integrity of the C-4 methylene protons for both **20** and **21** was demonstrated by an AB quartet similar to that found for other 1-substituted 6-phenyl-4*H*-*s*-triazolo[4,3-*a*][1,4]benzodiazepines (viz., **1**).[1] The corresponding C-4 protons of **19**, however, were represented by a very broad singlet suggesting a diminished conformational rigidity for this 1-oxygen-substituted derivative. A similar observation has been made for compound **2**.[14] The infrared carbonyl absorption at 1690 cm^{-1} and the ultraviolet maximum at 266 nm for **19** are compatible with data obtained for analogous mesoionic triazole derivatives.[13] For compound **20** a strong band at 1350 cm^{-1} in the infrared spectrum may be attributable to the C=S moiety;[15,16] the lack of carbonyl absorption for the NC(=O)CH_3 system of **21** has been documented for similar systems.[17]

Experimental Section

Melting points were taken in capillary tubes and are corrected. Ultraviolet spectra were determined on a Cary Model 14 spectrophotometer, IR spectra on a Perkin-Elmer Model 421 spectrophotometer, mass spectra at 70 eV on an Atlas Model CH-4 spectrometer, and NMR spectra on a Varian Model A-60A or XL-100 spectrometer. NMR peaks are recorded in parts per million downfield from tetramethylsilane. In general, only those NMR peaks which are either necessary for the structure proof or readily assignable to a specific proton or group of protons are reported; the integrated spectra are, however, in all cases in agreement with the assigned structures. Skellysolve B is a commercial hexane, bp 60–70 °C, made by Skelly Oil Co. Darco G-60 is an activated carbon prepared by Atlas Chemical Industries, Inc. The silica gel used for chromatography was obtained from E. Merck AG.

8-Chloro-1-methyl-6-phenyl-4*H*-*s*-triazolo[4,3-*a*][1,4]-benzodiazepine (1). A solution of **13**[18] (0.15 g) in $CHCl_3$ (10 mL) was refluxed for 10.5 h while a slow stream of air was bubbled through the mixture. The solution was evaporated and the residue chromatographed on 50 g of silica gel, using 5% MeOH–$CHCl_3$. The first material eluted from the column amounted to 98 mg and was crystallized from Et_2O to give recovered **13**; mp 149–150 °C. The second material eluted from the column amounted to 50 mg and was crystallized from EtOAc to give **1**; mp 228–229 °C (lit.[1] mp 228–228.5 °C).

Acetic Acid 2-(7-Chloro-5-phenyl-3*H*-1,4-benzodiazepin-2-yl)-1-methylhydrazide (4) from 1. A stirred solution of **1** (3.09 g, 0.01 mol) in dry CH_2Cl_2 (60 mL) was treated with trimethyloxonium fluoroborate (1.63 g, 0.011 mol), and the resulting mixture was stirred at ambient temperature, under N_2, for 18 h. The mixture was concentrated in vacuo and the residue was stirred with aqueous K_2CO_3 for 1 h 45 min. Methylene chloride was then added; the mixture became dark. It was stirred for an additional 30 min. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The CH_2Cl_2 solutions were combined, dried (K_2CO_3) and concentrated. The residue was crystallized from MeOH–EtOAc to give 0.36 g, mp 209–210 °C dec, 0.86 g, mp 207.5–209 °C dec, and 0.18 g, mp 203–206 °C dec, of **4**. The analytical sample gave the following data: mp 203–204 °C dec; UV (EtOH) end absorption, λ_{max} 227 (ϵ 31 850), 330 (2500) nm; IR (Nujol) 3180, 3050 (NH), 1625, 1580, 1560, 1480 (C=O/C=N/C=C) cm^{-1}; NMR [$(CD_3)_2NCDO$] δ 1.95 (s, 3, C(=O)CH_3), 3.11 (s, 3, NCH_3), ~4.29 (broad s, 2, (C-4)H_2); MS *m/e* (relative intensity) 340 (336, M^+), 297 (153), 269 (256), 268 (249), 255 (306), 253 (160).

Anal. Calcd for $C_{18}H_{17}ClN_4O$: C, 63.43; H, 5.03; Cl, 10.40; N, 16.44. Found: C, 63.20; H, 5.24; Cl, 10.13; N, 15.78.

Acetic Acid 2-(7-Chloro-5-phenyl-3*H*-1,4-benzodiazepin-2-yl)-1-methylhydrazide (4) and Acetic Acid 2-(7-Chloro-5-phenyl-3*H*-1,4-benzodiazepin-2-yl)-2-methylhydrazide (8) from 9. A mixture of **9** (2.87 g, 0.01 mol), methylhydrazine (2.01 g, 0.0436 mol), and methanol (100 mL) was stirred, under N_2, at ambient temperature for 2 h 15 min and concentrated in vacuo. The residue was twice mixed with benzene and concentrated in vacuo to remove residual methanol. The resulting residue was dissolved in dry THF (150 mL), cooled in an ice bath, and treated with a solution of Ac_2O (1.12 g) in THF (5 mL). This mixture was stirred, under N_2, at ambient temperature for 6 h and concentrated in vacuo. The residue was crystallized from EtOAc to give 1.35 g of **4**, mp 211.5–212.5 °C dec, which was identical with the authentic sample by IR (Nujol) and NMR [$(CD_3)_2NCDO$] comparison. The mother liquor from this crystallization was concentrated and chromatographed on silica gel (150 g) with 1.5% MeOH–98.5% $CHCl_3$. The first compound eluted from the column was crystallized from EtOAc to give 0.74 g, mp 214.5–215.5 °C dec, and 0.23 g, mp 212–213 °C dec, of **8**. The analytical sample gave the following data: mp 215–215.5 °C dec; UV (EtOH) end absorption, λ_{max} 231 (ϵ 29 750), 262 (19 150), 340 (2960), inflection 241 (10 720) nm; IR (Nujol) 3230, 3200, 3020 (NH), 1660, 1615, 1595, 1585, 1570, 1545 (C=O/C=N/C=C) cm^{-1}; NMR [$(CD_3)_2SO$] δ 1.99 (s, 3, C(=O)CH_3), 3.18 (s, 3, NCH_3); MS *m/e* (relative intensity) 340 (999, M^+), 323 (185), 282 (407), 253 (212).

Anal. Calcd for $C_{18}H_{17}ClN_4O$: C, 63.43; H, 5.03; Cl, 10.40; N, 16.44. Found: C, 63.25; H, 5.04; Cl, 10.36; N, 16.27.

Acetic Acid 2-(7-Chloro-5-phenyl-3*H*-1,4-benzodiazepin-2-yl)-2-methylhydrazide (8) from 7. A solution of **7** (0.299 g, 0.001 mol) in THF (15 mL) was cooled in an ice bath under

(10) This reaction has been used to prepare a variety of 4*H*-*s*-triazolo[4,3-*a*][1,4]benzodiazepines.[18]

(11) A similar observation has been reported for the 3-methyl peaks of the two 3-methyl-*s*-triazolo[4,3-*a*]pyridine methiodides: W. J. Paudler and R. J. Brumbaugh, *J. Heterocycl. Chem.*, **5**, 29 (1968).

(12) M. L. Casey, D. S. Kemp, K. G. Paul, and D. D. Cox, *J. Org. Chem.*, **38**, 2294 (1973), and references cited therein.

(13) For a comprehensive review of mesoionic systems see M. Ohta and H. Kato in "Nonbenzenoid Aromatics", J. P. Snyder, Ed., Academic Press, New York, N.Y., 1969, Chapter 4.

(14) J. B. Hester, Jr., P. F. VonVoigtlander, and A. D. Rudzik, *J. Med. Chem.*, in press.

(15) M. Ohta, H. Kato, and T. Kaneko, *Bull. Chem. Soc. Jpn.*, **40**, 579 (1967).

(16) K. T. Potts, S. K. Roy, and D. P. Jones, *J. Org. Chem.*, **32**, 2245 (1967).

(17) K. Ichimura and M. Ohta, *Bull. Chem. Soc. Jpn.*, **38**, 707 (1965).

(18) K. Meguro and Y. Kuwada, *Tetrahedron Lett.*, 4039 (1970).

N_2 and treated with Ac_2O (0.104 mL, 0.0011 mol). The mixture was stirred in the ice bath for 1 h and at ambient temperature for 2 h; it was then concentrated in vacuo. A solution of the residue in $CHCl_3$ was washed with dilute $NaHCO_3$ and dilute NaCl, dried (Na_2SO_4), and concentrated. The residue was crystallized from EtOAc to give 0.265 g of **8**; mp 214–215 °C. This material was identical with the authentic sample by IR (Nujol) and NMR [$(CD_3)_2SO$] spectral comparison.

Acetic Acid 2-(7-Chloro-5-phenyl-3*H*-1,4-benzodiazepin-2-yl)-1-methylhydrazide (4) from 11. A solution of **11** (0.5 g) in $CHCl_3$ (25 mL) and EtOAc (25 mL) was treated with H_2O (0.25 mL), stirred in air at ambient temperature for 43 h, and concentrated in vacuo. The residue was chromatographed on silica gel (40 g) with 2% MeOH–98% $CHCl_3$. The product eluted from the column was crystallized from MeOH–EtOAc to give 0.168 g, mp 203–205 °C dec, and 0.030 g, mp 203–206 °C dec, of **4**. This material was identical with the authentic sample by IR (Nujol) and NMR [$(CD_3)_2NCDO$] spectral comparison.

7-Chloro-2-(1-methylhydrazino)-5-phenyl-3*H*-1,4-benzodiazepine (7). A suspension of **9**[19] (8.6 g, 0.03 mol) in MeOH (600 mL) was treated with methylhydrazine (5.53 g, 0.12 mol) and stirred at ambient temperature for 2.5 h. A vigorous stream of N_2 was bubbled through the mixture during this period to remove liberated H_2S. The mixture was concentrated in vacuo to a small volume, diluted with ice water, and extracted with $CHCl_3$. The extract was washed with cold, dilute NaCl, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on silica gel (400 g) with 1.5% MeOH–98.5% $CHCl_3$. The product thus obtained was crystallized on the rotary evaporator at about 25 °C by replacing the $CHCl_3$ of a $CHCl_3$ solution first with EtOAc and then with Skellysolve B. The yield of **7** was 5.07 g, mp 166.5-173 °C, and 0.520 g, mp 175–176 °C. The analytical sample was recrystallized from EtOAc–Skellysolve B: mp 178.5–179.5 °C; UV (EtOH) end absorption, λ_{max} 232 (ϵ 21 400), 269 (18 300), 352 (2920) nm; IR (Nujol) 3290, 3180 (NH), 1645, 1590, 1575, 1565 (C=N/C=C) cm^{-1}; NMR ($CDCl_3$) δ 3.34 (s, 3, NCH_3), 4.33 (s, 2, NH_2).

Anal. Calcd for $C_{16}H_{15}ClN_4$: C, 64.32; H, 5.06; Cl, 11.87; N, 18.75. Found: C, 63.97; H, 4.99; Cl, 12.09; N, 18.84.

Acetic Acid 2-(7-Chloro-5-phenyl-3*H*-1,4-benzodiazepin-2-yl)hydrazide (6). A solution of Ac_2O (1.12 g, 0.011 mol) in THF (5 mL) was added to an ice-cold, stirred solution of **5** (2.85 g, 0.01 mol) in THF (150 mL), and the mixture was stirred at ambient temperature, under N_2, for 2 h 20 min. It was then poured into water and extracted with CH_2Cl_2. The extract was dried (K_2CO_3) and concentrated. The residue was crystallized from MeOH to give 2.29 g, mp 209–210 °C dec, and 0.39 g, mp 207–208 °C dec, of **6** (lit.[1] mp 199–200 °C dec). The product was identical with the authentic sample by IR (Nujol) spectral comparison.

8-Chloro-1,2-Dimethyl-6-phenyl-4*H*-s-triazolo[4,3-a]-[1,4]-benzodiazepinium Bromide (10, X = Br). A solution of **1**[1] (6.19 g, 0.02 mol) in dry CH_2Cl_2 (120 mL), under N_2, was treated with trimethyloxonium fluoroborate (3.25 g, 0.022 mol) and stirred at ambient temperature for 18 h. The resulting mixture was concentrated in vacuo, and the residue was suspended in dry Et_2O and stirred for about 30 min. The amorphous solid was collected by filtration and dried to give 8.39 g of crude 8-chloro-1,2-dimethyl-6-phenyl-4*H*-s-triazolo[4,3-a][1,4]benzodiazepinium fluoroborate. This material (**10**, X = BF_4, 4.11 g) was added to a solution of KBr (1.31 g) in water (2.6 mL). The resulting mixture was treated with absolute EtOH (12 mL), stirred for 1 h 45 min, and filtered. The filtrate was concentrated and the residue was crystallized from EtOH–EtOAc to give 0.655 g of **10** (X = Br); mp 233.5–235 °C. The analytical sample gave the following data: mp 235–236 °C; UV (EtOH) end absorption, λ_{max} 222 (ϵ 37 550), inflections 245 (16 150), 280 (4750) nm; IR (Nujol) 1610, 1600, 1570, 1490 (C=N/C=C) cm^{-1}; NMR [$(CD_3)_2NCDO$] δ 3.28 (s, 3, CCH_3), 4.28 (s, 3, NCH_3), 4.67, 5.47 (d, d, 2, J_{AB} = 13 Hz, C-4H_2); MS *m/e* 322, 308, 279, 273.

Anal. Calcd for $C_{18}H_{16}BrClN_4$: C, 53.54; H, 3.99; Br, 19.79; Cl, 8.78; N, 13.89. Found: C, 52.99; H, 3.74; Br, 19.83; Cl, 8.47; N, 13.86.

8-Chloro-2,4-dihydro-1,2-dimethyl-6-phenyl-1*H*-s-triazolo[4,3-a][1,4]benzodiazepine (11) from 10. A stirred suspension of **10** (X = BF_4) (6.15 g) in ice-cold absolute ethanol (60 mL), under N_2, was treated during about 1 min with sodium borohydride (0.567 g). The mixture was stirred for 15 min and poured into ice water. This mixture was extracted with $CHCl_3$. The extract was washed with cold, dilute brine, dried (K_2CO_3), and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 and crystallized at about 25 °C by replacing the CH_2Cl_2 with EtOAc under a stream of N_2 to give 1.58 g of product; mp 177–180 °C dec. This material was recrystallized from CH_2Cl_2–EtOAc to give 1.24 g of **11**, mp 184–186 °C dec, which was identical with the authentic sample by IR (Nujol) and NMR ($CDCl_3$) spectral analysis.

8-Chloro-2,4-dihydro-1,2-dimethyl-6-phenyl-1*H*-s-triazolo[4,3-a][1,4]benzodiazepine (11), 7-Chloro-2-(2-ethylidene-1-methylhydrazino)-5-phenyl-3*H*-1,4-benzodiazepine (14), and Acetic Acid 2-(7-Chloro-5-phenyl-3*H*-1,4-benzodiazepin-2-yl)-1-methylhydrazide (4) from 9. A mixture of **9**[19] (5.74 g, 0.02 mol), methylhydrazine (4.02 g, 0.0875 mol), and MeOH (200 mL) was stirred for 2.3 h and evaporated in vacuo at room temperature. A solution of the residue in 75 mL of CH_2Cl_2 was washed with cold water (4 × 50 mL) and saturated salt solution, dried ($MgSO_4$), and evaporated at room temperature. The residue was stirred for 2.5 h with 25 mL of acetaldehyde. The resulting suspension was evaporated and the residue extracted with Et_2O (4 × 50 mL). The resulting insoluble solid (2.1 g) was crystallized from ethyl acetate to give 1.5 g of **11** as yellow plates: mp 191–199 °C dec; UV (EtOH) λ_{max} 214 (ϵ 34 250), 267 (18 650), inflection 350 (1150) nm; IR (Nujol) 2780, 2700, 2600 (N–alkyl), 1640, 1610, 1595, 1575, 1560, 1485 (C=N/C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.53 (d, 3, J = 5 Hz, $CHCH_3$), 2.78 (s, 3, NCH_3), 3.96, 4.9 (d, d, 2, J_{AB} = 12 Hz, (C-4)H_2), 4.8 (q, 1, J = 5 Hz, $CHCH_3$); MS *m/e* 324 (M^+), 309, 273.

Anal. Calcd for $C_{18}H_{17}ClN_4$: C, 66.56; H, 5.28; Cl, 10.91; N, 17.25. Found: C, 66.72; H, 5.18; Cl, 10.89; N, 17.19.

The Et_2O extract was concentrated to half volume and allowed to crystallize to give 1.0 g of a solid. This operation was repeated to give a second (0.9 g) and third (0.45 g, mp 189–195 °C) crop. The third crop was recrystallized from EtOAc to give **14** as colorless rods: mp 199–200 °C; UV (EtOH) λ_{max} 233 (ϵ 26 000), 293 (27 200), 347 (4400), inflection 248 (22 700), 279 (23 100) nm; IR (Nujol) 1630, 1600, 1575, 1535, 1485 (C=N/C=C) cm^{-1}; NMR ($CDCl_3$) δ 2.07 (d, 3, J = 5 Hz, $CHCH_3$), 3.4 (s, 3, NCH_3), 7.07 (q, 1, J = 5 Hz, $CHCH_3$); MS *m/e* 324 (M^+), 309, 281.

Anal. Calcd for $C_{18}H_{17}ClN_4$: C, 66.56; H, 5.28; Cl, 10.91; N, 17.25. Found: C, 66.69; H, 5.05; Cl, 10.77; N, 17.41.

The first two crops of solid and the filtrates were combined and chromatographed on silica gel (580 g), using 3% MeOH–96% $CHCl_3$–1% Et_3N. The first material eluted from the column was recrystallized from EtOAc to give 0.573 g of additional **14**; mp 199–200 °C. Subsequent fractions contained 2.86 g of a mixture of compounds **4**, **14**, and **11** which was followed by pure **4**. This material was recrystallized from Et_2O and then EtOAc to give 0.185 g of **4**; mp 209 °C dec. The IR (Nujol) and NMR [$(CD_3)_2NCDO$)] spectra of this material were identical with those of an authentic sample.

Anal. Calcd for $C_{18}H_{17}ClN_4O \cdot {}^1/_4EtOAc$: C, 62.89; H, 5.28; Cl, 9.77; N, 15.44. Found: C, 62.85; H, 5.28; Cl, 10.10; N, 15.87.

7-Chloro-2-(2-ethylidenehydrazino)-5-phenyl-3*H*-1,4-benzodiazepine (13). Acetaldehyde (25 mL) was added to solid **5** (5.1 g, 0.018 mol); the mixture refluxed gently and a thick suspension resulted. This was stirred for 2 h and evaporated in vacuo at 30 °C. The residue was dissolved in 800 mL of ether and the mixture filtered to remove some insoluble material. The filtrate was concentrated to 50 mL and crystallized to give 2.6 g of **13**; mp 148–150 °C. The analytical sample was recrystallized from Et_2O: mp 151–152 °C (lit.[20] mp 162–164 °C); UV (EtOH) inflections 214 (ϵ 29 800), 230 (23 650), λ_{max} 260 (26 250), 335 (2500) nm; IR (Nujol) 3300 (NH), 1645, 1615, 1575, 1560, 1485 (C=N/C=C) cm^{-1}; NMR ($CDCl_3$) δ 2.03 (d, 3, J = 5 Hz, $CHCH_3$), 4.47 (s, 2, (C-4)H_2), 7.91 (q, 1, J = 5 Hz, $CHCH_3$), 8.5 (s, 1, NH); MS *m/e* 310 (M^+), 295, 268, 266, 241, 165.

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Anal. Calcd for $C_{17}H_{15}ClN_4$: C, 65.70; H, 4.87; Cl, 11.40; N, 18.03. Found: C, 65.60; H, 5.05; Cl, 11.34; N, 17.87.

7-Chloro-2-(2-ethylidene-1-methylhydrazino)-5-phenyl-3*H*-1,4-benzodiazepine (14). Compound **7** (0.5 g, 0.0017 mol) was treated with acetaldehyde (5 mL), stirred for 2 h at ambient temperature, and concentrated at ambient temperature. The residue was triturated with cold EtOAc to give 0.399 g of **14**; mp 199–200 °C. A second crop, 0.050 g, mp 198–199 °C, was obtained by concentrating the mother liquors. A mixture melting point of this material with an authentic sample of **14** was not depressed; the IR (Nujol) spectra were identical.

X-ray Study of 14. Crystal data for racemic **14** ($C_{18}H_{17}ClN_4$) were as follows: monoclinic, space group $P2_1/c$, $Z = 4$, $a = 15.414$ (2) Å, $b = 7.158$ (1) Å, $c = 16.270$ (2) Å, $\beta = 113.42$ (1)°, $D_{measd} = 1.31$ g/cm^3, $D_{calcd} = 1.31$ g/cm^3, μ(Cu Kα) = 19.7 cm^{-1}, 2757 reflections of which 2115 had intensities greater than one standard deviation. Intensity data for all reflections with $2\theta < 138°$ were collected by using the step-scan technique[21] at low temperature (about −155 °C) on a Syntex $P\bar{1}$ diffractometer controlled by an IBM 1800 computer using graphite-monochromatized Cu Kα radiation ($\lambda = 1.5418$ Å). Data were corrected for systematic errors including absorption.[22] Coordinates and anisotropic thermal parameters of heavier atoms were refined by multiple matrix least squares. The final agreement index R [$R = \sum||F_o| - |F_c||/\sum|F_o|$] was 0.111. For the 1492 most significant reflections ($F_o^2 > 3\sigma(F_o^2)$), R was 0.073. The standard deviation of fit was 2.29. All calculations were carried out on an IBM 370 computer by using the CRYM system of crystallographic programs.[23]

8-Chloro-1,3-dimethyl-6-phenyl-4*H*-*s*-triazo[4,3-*a*][1,4]-benzodiazepinium Tosylate (15, X = $C_7H_7SO_3$). A stirred mixture of **7** (5.58 g, 0.02 mol), ethyl orthoacetate (22.6 mL), and $CHCl_3$ (100 mL), under N_2, was treated with *p*-toluenesulfonic acid hydrate (4.19 g, 0.022 mol) and kept at ambient temperature for 4 h 10 min and at reflux for 25 min. The cooled reaction mixture was concentrated in vacuo and the residue was mixed with Et_2O and allowed to crystallize. The solid was collected by filtration, washed with Et_2O, and recrystallized from EtOH–EtOAc (Darco) to give 7.51 g, mp 118 °C dec, 0.821 g, mp 108 °C dec, and 0.653 g, mp 102 °C dec, of **15** (X = $C_7H_7SO_3$). The analytical sample gave the following data: mp 149–152 °C dec with softening at 113 °C; UV (EtOH) end absorption, λ_{max} 223 (ϵ 50 400), inflections 250 (13 200), 262 (8600), 266 (8030), 271 (7280), 277 (6020), 285 (5020), 295 (3180); IR (Nujol) 1735 (EtOAc), 1610, 1575, 1490 (C=N/C=C) cm^{-1}; NMR [$(CD_3)_2NCDO$] δ 2.31 (s, 3, $CH_3C_6H_4SO_3$), 2.87 (s, 3, CCH_3), 4.36 (s, 3, NCH_3), 4.64, 5.95 (d, d, 2, J_{AB} = 14 Hz, (C-4)H_2); MS *m/e* (relative intensity) 322 (227), 321 (589), 307 (347), 278 (264), 272 (187), 218 (359).

Anal. Calcd for $C_{25}H_{23}ClN_4O_3S{\cdot}C_4H_8O_2$: C, 59.73; H, 5.34; Cl, 6.08; N, 9.61; S, 5.50; EtOAc, 15.11. Found: C, 59.80; H, 5.37; Cl, 6.20; N, 9.85; S, 5.79; EtOAc, 13.8.

8-Chloro-1,3-dimethyl-6-phenyl-4*H*-*s*-triazolo[4,3-*a*]-[1,4]benzodiazepinium Chloride Sesquihydrate (15, X = Cl). A solution of **15** (X = $C_7H_7SO_3$, 1.5 g) in water (25 mL) was poured through a column containing 20 g of Amberlite IRA 400 in the chloride form. The column was eluted with water. The resulting solution was concentrated in vacuo and the residue was redissolved in absolute EtOH and concentrated. The resulting material was crystallized from MeOH–EtOAc to give 1.06 g of **15** (X = Cl). The analytical sample gave the following data: mp 170.5 °C dec; UV (EtOH) λ_{max} 223 (ϵ 38 000), inflections 247 (13 720), 265 (7660), 285 (4870) nm; IR (Nujol) 3340, 3240 (OH), 1610, 1575, 1490 (C=N/C=C) cm^{-1}; NMR [$(CD_3)_2SO$] δ 2.79 (s, 3, CCH_3), 4.26 (s, 3, NCH_3), 4.48, 5.89 (d, d, 2, J_{AB} = 14 Hz, (C-4)H_2).

Anal. Calcd for $C_{18}H_{16}Cl_2N_4{\cdot}1.5H_2O$: C, 55.97; H, 4.96; Cl, 18.36; N, 14.50; H_2O, 6.99. Found: C, 56.02; H, 4.55; Cl, 18.85; N, 14.32; H_2O, 7.38.

8-Chloro-3-methyl-6-phenyl-4*H*-*s*-triazolo[4,3-*a*][1,4]-benzodiazepinium Chloride (16, X = Cl). A stirred solution of **7** (2.40 g) and ethyl orthoformate (6.4 mL) in $CHCl_3$ (64 mL) was treated with H_2SO_4 (1.6 g) and kept at ambient temperature, under N_2, for 18 h. The solid was collected by filtration, washed with $CHCl_3$, and dried to give 3.87 g of crude **16** (X = HSO_4). A solution of this material in water was poured onto a column of Amberlite IRA-400 resin in the chloride form. The column was eluted with water and the eluate was concentrated in vacuo. A solution of the residue in absolute EtOH was concentrated. The resulting material appeared to be a mixture of **16** (X = Cl) and its hydrochloride salt. It was therefore dissolved in a small amount of saturated aqueous NaCl, neutralized with $NaHCO_3$, and extracted four times with $CHCl_3$. The extract was washed with brine, dried ($NaSO_4$), and concentrated in vacuo. The residue was crystallized from EtOH–EtOAc to give 1.05 g, mp 213–214 °C dec, and 0.864 g, mp 207–209 °C dec, of **16** (X = Cl). The analytical sample gave the following data: mp 214–217 °C dec; UV (EtOH) end absorption, λ_{max} 224 (ϵ 35 050), inflections 250 (12 200), 265 (6950), 285 (4050) nm; IR (Nujol) 3050 (HC=), 1610, 1565, 1540, 1480 (C=N/C=C) cm^{-1}; NMR [$(CD_3)_2NCDO$, 100 MHz] δ 4.46 (s, 3, NCH_3), ~5.46 (broad s, 2, (C-4)H_2), 7.54 (m, 6, Ar**H**), 8.06 (dd, 1, J = 9 Hz, 2 Hz, (C-9)H), 8.56 (d, 1, J = 9 Hz, (C-10)H), 10.59 (s, 1, (C-1)H); MS *m/e* (relative intensity) 308 (548), 294 (999), 259 (837).

Anal. Calcd for $C_{17}H_{14}Cl_2N_4$: C, 58.97; H, 4.37; Cl, 20.48; N, 16.18. Found: C, 58.20; H, 4.55; Cl, 18.52; N, 14.67; H_2O, 0.92; EtOAc, 9.72. The analytical data was recalculated based on the observed H_2O and EtOAc: C, 59.19; H, 4.01; Cl, 20.85; N, 16.33.

7-Chloro-2,3-dihydro-2-(methylimino)-5-phenyl-1*H*-1,4-benzodiazepine-1-carbonitrile (18). A stirred solution of **7** (1.50 g, 0.005 mol) and triethyl orthoformate (3.7 g, 0.025 mol) in $CHCl_3$ (40 mL) was treated with H_2SO_4 (1.0 g) and kept, under N_2, at ambient temperature for 18 h. The white crystalline product was collected by filtration, washed with $CHCl_3$, and suspended in a mixture of $CHCl_3$ and water. This mixture was neutralized with $NaHCO_3$ and washed with $CHCl_3$. The aqueous layer was made strongly basic with 15% NaOH. The purple material which formed was extracted with $CHCl_3$. The extract was washed with brine, dried (K_2CO_3), and concentrated in vacuo. (The $CHCl_3$ extract was initially purple, but, on standing, the color faded and became tan.) The residue was crystallized from EtOAc–Skellysolve B to give 0.426 g of **18**; mp 184–190 °C dec. The analytical sample gave the following data: mp 186–188 °C dec; UV (EtOH) end absorption, λ_{max} 228 (ϵ 31 000), inflections 255 (13 950), 277 (5620), 305 (2415) nm; IR (Nujol) 2230 (C≡N), 1690 (C=N), 1605, 1575, 1560 (C=N/C=C) cm^{-1}; NMR ($CDCl_3$) δ 3.43 (s, 3, NCH_3), ~4.25 (broad s, (C-4)H_2); MS *m/e* 308 (M^+), 267, 239, 232, 205.

Anal. Calcd for $C_{17}H_{13}ClN_4$: C, 66.13; H, 4.24; Cl, 11.48; N, 18.15. Found: C, 66.08; H, 4.27; Cl, 11.48; N, 18.08.

1-Amino-8-chloro-3-methyl-6-phenyl-4*H*-*s*-triazolo[4,3-*a*][1,4]benzodiazepinium Chloride (17, X = Cl). A stirred mixture of **7** (8.97 g, 0.03 mol) and dioxane (75 mL) was cooled, under N_2, in an ice bath and treated during 20 min with a solution of cyanogen bromide (3.18 g) in dioxane (30 mL). This mixture was kept at ambient temperature for 17 h and at 69–79 °C for 3 h. It was then cooled and filtered. The solid was washed with dioxane, dissolved in about 500 mL of warm, absolute EtOH, decolorized with Darco G60, and crystallized by slowly concentrating the solution in vacuo at about 25 °C. This gave 5.11 g, mp 263–265 °C dec, and 1.11 g, mp 258–261 ° dec, of **17** (X = Br). A mixture of this material (1.0 g) and water (40 mL) was filtered, and the filtrate was passed through a column of Amberlite IRA-400 resin in the chloride form. The column was eluted with water; the eluate was concentrated in vacuo and the residue was dissolved in absolute EtOH and concentrated. The resulting material was crystallized from EtOH to give 0.207 g, mp 264.5–266.5 °C dec, and 0.320 g, mp 260.5–262 °C dec, of **17** (X = Cl). The analytical sample gave the following data: mp 269 °C dec; UV (EtOH) λ_{max} 217 (ϵ 33 000), 257 (14 200) nm; IR (Nujol) 3180 (NH), 3020 (=CH, NH), 1640, 1605, 1580, 1575, 1495 (C=N, C=C, NH) cm^{-1}; NMR (D_2O) δ 4.03 (s, 3, NCH_3), 4.37, 5.4 (d, d, 2, J_{AB} = 15 Hz, (C-4)H_2); MS *m/e* (relative intensity) 323 (675).

Anal. Calcd for $C_{17}H_{15}Cl_2N_5$: C, 56.68; H, 4.20; Cl, 19.68; N, 19.44. Found: C, 56.20; H, 4.37; Cl, 19.68; N, 19.17.

8-Chloro-1-hydroxy-3-methyl-6-phenyl-4*H*-*s*-triazolo-[4,3-*a*][1,4]benzodiazepinium Hydroxide Inner Salt (19). Phosgene (0.4 mL, 0.0055 mol) was evaporated during 45 min into an ice-cold, stirred mixture of **7** (1.5 g, 0.005 mol), THF (15 mL), and Et_3N (1.53 mL, 0.011 mol). The mixture became very thick

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(22) W. R. Busing and H. A. Levy, *Acta Crystallogr.*, **10**, 180 (1975).
(23) The CRYM crystallographic programs were by D. J. Duchamp, The Upjohn Company, Kalamazoo, Mich. 49001.

and after 1 h additional THF (10 mL) was added. It was allowed to warm to ambient temperature and stand for 5 h 30 min; it was then poured into ice water. This mixture was neutralized with $NaHCO_3$ and extracted with $CHCl_3$. The extract was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was crystallized from MeOH–EtOAc to give 1.1 g, mp 285–286 °C, and 0.184 g, mp 275–276 °C (79.1% yield), of **19**. The analytical sample gave the following data: mp 286–288 °C dec; UV (EtOH) λ_{max} 221 (ϵ 33 720), 266 (15 090); IR (Nujol) 1690, 1660 (sh) (C=O), 1620, 1610, 1590, 1575, 1565, 1510 (C=N/C=C) cm^{-1}; NMR [$(CD_3)_2NCDO$] δ 3.94 (s, 3, NCH_3), ~4.9 (broad s, 2, (C-4)H_2); MS *m/e* 324, 296, 282, 253.

Anal. Calcd for $C_{17}H_{13}ClN_4O$: C, 62.87; H, 4.03; Cl, 10.92; N, 17.25. Found: C, 62.23; H, 4.06; Cl, 10.93; N, 17.17.

8-Chloro-1-mercapto-3-methyl-6-phenyl-4*H*-*s*-triazolo[4,3-*a*][1,4]benzodiazepinium Hydroxide Inner Salt (20). A stirred mixture of **7** (4.48 g, 0.015 mol), triethylamine (4.68 mL, 0.033 mol), and THF (60 mL) was cooled, under N_2, in salt–ice bath and treated, dropwise during 1 h 20 min with a solution of thiophosgene (1.26 mL) in THF (30 mL). The mixture was allowed to warm slowly to ambient temperature, stand for 15 h 40 min, and finally reflux on the steam bath for 1 h 10 min. The cooled mixture was poured into ice water. The solid was collected by filtration, dissolved in $CHCl_3$, washed with brine, and dried (Na_2SO_4). The aqueous filtrate was concentrated in vacuo to remove THF and extracted with $CHCl_3$. The extract was washed with brine and dried (Na_2SO_4). The $CHCl_3$ solutions were combined and concentrated and the residue was chromatographed on silica gel (300 g) with 2% MeOH–98% $CHCl_3$. The product thus obtained was recrystallized from CH_2Cl_2–MeOH to give 1.33 g, mp 261.5–267 °C dec with softening at 253 °C, and 1.94 g, mp 258–267 °C dec with softening at 245 °C. The analytical sample gave the following data: mp 258–262 °C dec with softening at 245 °C; UV (EtOH) λ_{max} 219.5 (ϵ 46 100), 278 (8250), inflections 245 (19 150), 260 (11 250), 310 (4200) nm; IR (Nujol) 1615, 1600, 1565, 1490 (C=N/C=C), 1360, 1350, 1335, 1320, 1310, 1195, 1125, 1000 (=CH, C=S, etc.) cm^{-1}; NMR [$(CD_3)_2SO$] δ 3.95 (s, 3, NCH_3), 4.24, 5.63 (d, d, 2, J_{AB} = 14 Hz, (C-4)H_2); MS *m/e* (relative intensity) 340 (999).

Anal. Calcd for $C_{17}H_{13}ClN_4S$: C, 59.91; H, 3.84; Cl, 10.40; N, 16.44; S, 9.41. Found: C, 59.99; H, 3.99; Cl, 10.67; N, 16.81; S, 9.38.

1-Acetamido-8-chloro-3-methyl-6-phenyl-4*H*-*s*-triazolo[4,3-*a*][1,4]benzodiazepinium Hydroxide Inner Salt Hydrate (21). Compound **17** (X = Cl) (1.43 g, 0.00396 mol) was added, under N_2, to a stirred, ice-cold mixture of triethylamine (8 mL) and acetic anhydride (4 mL); the resulting mixture was kept in the ice bath for 6 h 25 min, treated with absolute EtOH (10 mL), and allowed to warm slowly to ambient temperature during 15 h. The mixture was concentrated in vacuo and the residue was mixed with dilute $NaHCO_3$ and extracted with $CHCl_3$. The extract was washed with brine, dried (K_2CO_3), and concentrated in vacuo. The residue was dissolved in MeOH, decolorized with Darco, and crystallized from MeOH–EtOAc (wet) to give 0.317 g, mp 170–171 °C dec, and 0.264 g, mp 170–171 °C dec, of **21**. The analytical sample gave the following data: mp 169–171 °C dec; UV (EtOH) end absorption, λ_{max} 221 (ϵ 38 200), inflection 272 (11 550) nm; IR (Nujol) 3510, 3370 (H_2O), 1640 (sh), 1620, 1605, 1600, 1580, 1515 (C=O, C=N, C=C) cm^{-1}; NMR ($CDCl_3$) δ 2.10 (s, 3, C(=O)CH_3), 4.02 (s, 3, NCH_3), 4.18, 5.36 (d, d, 2, J_{AB} = 14 Hz, (C-4)H_2); MS *m/e* (relative intensity) 365 (141), 350 (999).

Anal. Calcd for $C_{19}H_{16}ClN_5O$: C, 62.38; H, 4.41; Cl, 9.69; N, 19.14. Found: C, 60.18; H, 4.76; Cl, 9.48; N, 18.44; H_2O, 4.04. Analytical data corrected for water: C, 62.71; H, 4.50; Cl, 9.88; N, 19.22.

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Registry No. **1**, 28981-97-7; **3**, 55775-75-2; **4**, 41154-37-4; **5**, 18091-89-9; **6**, 28910-89-6; **7**, 56167-78-3; **8**, 70524-39-9; **9**, 4547-02-8; **10** (X = BF_4), 41506-84-7; **10** (X = Br), 41154-41-0; **11**, 41154-39-6; **13**, 41212-87-7; **14**, 70524-40-2; **15** (X = $C_7H_7SO_3$), 56167-86-3; **15** (X = Cl), 56167-87-4; **16** (X = HSO_4), 67171-61-3; **16** (X = Cl), 56167-84-1; **17** (X = Br), 56167-82-9; **17** (X = Cl), 56167-83-0; **18**, 56167-89-6; **19**, 56167-80-7; **20**, 56167-79-4; **21**, 56167-88-5.

Nicotinic Acid Crown Ethers.[1] Synthesis, Reactions, and Complexation of Nicotinonitrile Macrocycles

George R. Newkome* and Toshio Kawato[2]

Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana 70803

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2,6-Dichloronicotinamide (**6**), prepared from the corresponding disubstituted nicotinic acid, was dehydrated with refluxing thionyl chloride to give the nitrile **8**, which was subsequently converted into the 1:1 macrocyclic nicotinonitriles **9**. Isomeric macrocyclic dimers **10** were also isolated from the reaction. NMR and mass spectral data were used to ascertain the macrocyclic structures. Eu(fod)$_3$ shift reagent was employed to demonstrate that the predominant site of europium ion coordination in these nitrile macrocycles is the central bridging ethereal oxygens. Reduction of **9b** with lithium aluminum hydride or Vitride gave fragmentation of the macrocyclic ring nucleus resulting in formation of pentaethylene glycol and reduction products derived from the pyridine nucleus.

The synthesis and reactions of 1,4-dihydropyridines have been demonstrated to be a dynamic area in organic and bioorganic chemistry in view of their potential simplistic mimicking of the pyridine-linked nucleotide's reactions.[3,4] 1-Metallodihydropyridines (**1**), prepared from pyridine upon treatment with various reducing agents such as $LiAlH_4$,[5a,b] ZnH_2,[5c] or organometallic reagents,[3] have been

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