were saponified with a mixture of 1 N NaOH and EtOH by refluxing for 30–60 min. Cooling and acidification with HCl precipitated crude **7–9**.

4-R^1-5-Amino-3-benzylaminobenzoic Acids 10, 13, and 16 (Table IV). Method C. To a solution of $Na_2S_2O_4$ (16.1 g, 80 mmol) in H_2O (100 mL) NH_3 (55 mL, 25% in H_2O) was added followed by **7** (9.1 g, 25 mmol) in portions. After heating on a steam bath for 1 h, H_2O (100 mL) followed by 4 N HCl (100 mL) was added and the heating continued for 15 min. Cooling completed the precipitation of crude **10**.

Method D. **8** and **9** were reduced using a previously described procedure (see ref 5, method E), except that the heating following the acidification was omitted.

4-R^1-3-R^2-5-NHCOR^3-Benzoic Acids 26–53 (Table I). Method E. A mixture of **10**, **11** and **12**,[2] **13**, **14** and **15**,[3] or **17**–**25**[3] and HCOOH (10–15 mL/g of starting amine) was heated on a steam bath for a few minutes followed by stirring at ambient temperature for 2.5–24 h. Cooling and/or dilution with H_2O precipitated the crude reaction product. For **26** the reaction mixture was evaporated in vacuo and crude **26** obtained on trituration with Et_2O.

Method F. A mixture of **10**, **14**,[3] **16**, **18**,[3] or **19**,[3] Ac_2O (1 mL/g of starting amine), and AcOH (5–10 mL/g of starting amine) was heated on a steam bath for 1–5 h. Dilution with H_2O precipitated the crude reaction product. Occasionally a larger amount of Ac_2O (5–10 mL/g of amine) was used, omitting the dilution with AcOH, and usually performing the reaction at ambient temperature.

Method G. A mixture of **10** (3.35 g, 10 mmol), KOCN (1.0 g, 12.3 mmol), and AcOH (50 mL) was stirred at ambient temperature for 5 h. Dilution with H_2O (250 mL) precipitated crude **28**. The purification was performed via the Na salt as described in ref 1, method K.

Method H. To a stirred solution of **10** (1.67 g, 5 mmol) in Me_2CO (25 mL) the appropriate alkyl isocyanate (5 mmol) was added, in case of MeNCO as a 5% solution in Me_2CO. Stirring at ambient temperature for a further 18–60 h and cooling precipitated crude **29** or **30**.

Method I. A mixture of **19**[3] (0.7 g, 2 mmol), the appropriate acyl chloride or anhydride (2.8–3 mmol), pyridine (0.5 mL), and $CHCl_3$ (7 mL) was refluxed for 2–4 h. In the case of **43** the mixture was left at ambient temperature for 60 h. Evaporation in vacuo and trituration with aqueous EtOH yielded crude **43–45**.

Method J. A mixture of **19**[3] (0.7 g, 2 mmol), C_6H_5COCl (0.42 g, 3 mmol), and saturated $NaHCO_3$ (7 mL) was heated on a steam bath for 3 h. After cooling, the precipitated Na salt of **46** was isolated and worked up as described in ref 1, method K.

Method K. A mixture of **44** (0.85 g, 2 mmol) and Me_2NH (10 mL, 20% in H_2O) was left at ambient temperature for 60 h. Evaporation in vacuo and treatment of the residue with concentrated HCl (5 mL) yielded, after cooling, crude **47** as its hydrochloride.

Alkyl 4-Benzoyl-3-benzyloxy-5-*N*-alkylformamidobenzoates 58–59 (Table III). Method L. To a stirred mixture of NaH (0.35 g, 50% in oil) and HMPA (12 mL), **41** (1.0 g, 2.7 mmol) was added in portions followed by the appropriate alkyl iodide (15–16 mmol). The mixture was stirred at ambient temperature for 20 h and crude **58–59** was precipitated on dilution with 0.25 N HCl (50 mL).

4-Benzoyl-3-benzyloxy-5-*N*-alkylformamidobenzoic Acids 60 and 61 (Table III). Method M. To a stirred mixture of **58** or **59** (1 mmol) and EtOH (6 mL), 1 N NaOH (1.1 mL) was added during about 5 min. After stirring for 5–6 h at ambient temperature crude **60** or **61** was precipitated by addition of 1 N HCl (1.5 mL).

4-Benzoyl-3-benzyloxy-5-alkylaminobenzoic Acids 62 and 63 (Table III). Method N. A mixture of **58** or **59** (1.5 mmol), 4 N NaOH (5 mL), and EtOH (5 mL) was refluxed for 3–4 h. Cooling and addition of 4 N HCl (6 mL) precipitated crude **62** or **63**.

4-Benzoyl-3-benzyloxy-5-dimethylaminobenzoic Acid (64) (Table III). Method O. A mixture of **19**[3] (1.73 g, 5 mmol), MeI (2.0 mL), and MeOH (25 mL) was refluxed for 42 h. After 16 and 24 h, additional MeI (each time 2 mL) was added. The resulting solution was evaporated in vacuo. To the residue 2 N NaOH (20 mL) was added and the mixture was heated on a steam bath for 1.5 h. After cooling, the precipitated Na salt of **64** was isolated and worked up as described in ref 1, method K.

5-Benzyloxy-7-carboxy-4-phenyl-2(3*H*)-quinazolinone (54) (Table II). Method P. A mixture of **19**[3] (2.2 g, 6.4 mmol), KOCN (0.75 g, 9.2 mmol), and AcOH (30 mL) was stirred at ambient temperature for 24 h. Cooling completed the precipitation of crude **54**.

3-Alkyl-5-benzyloxy-7-carboxy-4-phenyl-2(3*H*)-quinazolinones 55–57 (Table II). Method Q. A mixture of **19**[3] (0.7 g, 2 mmol), the appropriate alkyl isocyanate (2.7–3.3 mmol), pyridine (0.3 mL), and benzene (7 mL) was left at ambient temperature for **24** h or, in the case of **55**, refluxed for 2 h. Evaporation in vacuo and trituration with 1 N AcOH yielded crude **55–57**.

Acknowledgment. The authors are greatly indebted to the staff of the Department of Pharmacology for the diuretic screening of the compounds described in this paper.

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Antileukemic Activity of Derivatives of 1-Phenyl-2,5-dimethyl-3,4-bis(hydroxymethyl)pyrrole Bis(*N*-methylcarbamate)[1]

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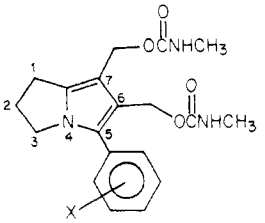
Treatment of *N*-aryl-*N*-acetylalanine derivatives, **3**, with acetic anhydride–dimethyl acetylenedicarboxylate gave the dimethyl *N*-aryl-2,5-dimethylpyrrole-3,4-dicarboxylates, **4**. Reduction of **4** and acylation of **5** gave **2a–j** and **6**. All of the title compounds **2a–j** and **6** showed significant reproducible activity in the P388 in vivo antileukemic assay.

During the course of our continuing search for new "lead" structures that possess antineoplastic activity, we prepared some bis(*N*-methylcarbamoyl) derivatives (**1**) of 2,3-dihydro-5-phenyl-6,7-bis(hydroxymethyl)-1*H*-pyrrolizine.[2b] The significant reproducible activity shown by these compounds against P388 lymphocytic leukemic in vivo emphasized the potentially important role the acylated vinylogous carbinolamine moiety plays in determining antineoplastic activity.

The nature of the X substituent in the pyrrolizines, **1**,



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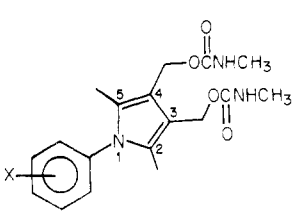

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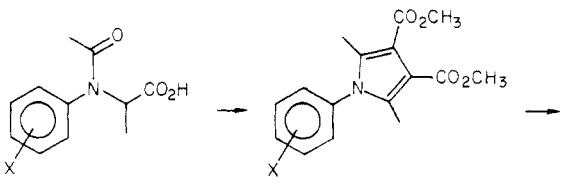
was shown to have a significant effect upon the chemical reactivity and biological activity of the system.[2b] The chemical reactivity of **1** toward nucleophiles was found to decrease as the electron-withdrawing power of the C-5 substituent increased; clearly the reactivity of this system was dependent upon the π-electron density in the pyrrole ring and upon the ability of the C-5 substituent to stabilize a developing positive charge during the displacement of the ester moieties (via *O*-alkyl cleavage).

In order to evaluate those factors which influence antineoplastic activity and toxicity in the acylated vinylogous carbinolamine system, we prepared a series of bis(*N*-methylcarbamoyl) derivatives (**2**) of 1-phenyl-2,5-dimethyl-3,4-bis(hydroxymethyl)pyrrole. The reactivity of **2** compared to **1** should be modified because of the electronic perturbations in the pyrrole caused by shifting the phenyl ring from the pyrrole 2 position to the 1 position. In addition, electron-donating X substituents cannot participate as effectively in the resonance stabilization of developing positive charges in reactions of **2** compared to **1**. The carbamate function was chosen as the esterifying moiety in **2** because of its potential increased resistance to esterase hydrolysis in vivo.[2b]

Chemistry. The synthesis of derivatives of **2** was readily accomplished starting from the appropriately substituted aniline. Acetylation of the aniline followed by *N*-alkylation with ethyl 2-bromopropionate and saponification of the resulting ester gave **3**. Treatment of **3** with acetic anhydride and dimethyl acetylenedicarboxylate (DMAD) gave **4**; the reaction proceeded via a 1,3-dipolar cycloaddition reaction of DMAD with a mesoionic oxazolone[3] intermediate generated in situ. Reduction of **4** ($LiAlH_4$) and subsequent acylation of the product diol, **5**, with methyl isocyanate gave **2**. Treatment of the diol **5a** with acetic anhydride gave the diacetate, **6**. The yields, melting points, and recrystallizing solvents are summarized in Table I. IR and NMR spectra were consistent with the structures.



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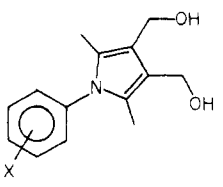

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a, X = 4′-OCH_3
b, X = 4′-OC_2H_5
c, X = 3′,4′-OCH_2O-
d, X = 4′-CH_3
e, X = 4′-*n*-C_4H_9
f, X = H
g, X = 4′-F
h, X = 4′-Cl
i, X = 4′-Br
j, X = 3′,4′-Cl_2

Table I

Compd (% yield)	Mp, °C (solvent)[a]	Formula[b]
2a (76)	156-158 dec (A)	$C_{19}H_{25}N_3O_5$
2b (89)	152-154 dec (A)	$C_{20}H_{27}N_3O_5$
2c (82)	168-170 dec (A)	$C_{19}H_{23}N_3O_6$
2d (81)	141-143 dec (A)	$C_{19}H_{25}N_3O_4$
2e (20)	179-181 dec (A)	$C_{22}H_{31}N_3O_4$
2f (90)	144-146 dec (A)	$C_{18}H_{23}N_3O_4$
2g (83)	159-161 dec (A)	$C_{18}H_{22}N_3O_4F$
2h (94)	179-181 dec (A)	$C_{18}H_{22}N_3O_4Cl$
2i (80)	183-185 dec (A)	$C_{18}H_{22}N_3O_4Br$
2j (85)	152-154 dec (A)	$C_{18}H_{21}N_3O_4Cl_2$
3a (70)	197-201 (B)	
3b (78)	195-198 (B)	
3c (64)	205-207.5 (B)	
3d (55)	166-169.5 (C)	
3e (87)	120.5-124.5 (B)	
3f (69)	141-145 (C)[c]	
3g (70)	132.5-136 (B)	
3h (70)	120-123 (A)	
3i (43)	120-124 (A)	
3j (61)	146.5-149 (A)	
4a (98)	75-76 (D)	$C_{17}H_{19}NO_5$
4b (83)	129-130 (E)	$C_{18}H_{21}NO_5$
4c (87)	130.8-131.8 (E)	$C_{17}H_{17}NO_6$
4d (90)	118.5-120.5 (E)	$C_{17}H_{19}NO_4$
4e (71)	93-94 (E)	$C_{20}H_{25}NO_4$
4f (88)	86-87 (E)[d]	
4g (90)	108.8-109.8 (E)	$C_{16}H_{16}NO_4F$
4h (99)	109.5-110.5 (E)	$C_{16}H_{16}NO_4Cl$
4i (92)	139-140 (E)	$C_{16}H_{16}NO_4Br$
4j (95)	83-91.5 (E)	$C_{16}H_{15}NO_4Cl_2$
5a (91)	143-145 dec (F)	$C_{15}H_{19}NO_3$
5b (83)	134-136 dec (F)	$C_{16}H_{21}NO_3$
5c (82)	143-145 dec (F)	$C_{15}H_{17}NO_4$
5d (91)	157-159 dec (F)	$C_{15}H_{19}NO_2$
5e (89)	Syrup	
5f (93)	111-112 dec (F)	$C_{14}H_{17}NO_2$
5g (79)	156-158 dec (F)	$C_{14}H_{16}NO_2F$
5h (55)	163-165 dec (F)	$C_{14}H_{16}NO_2Cl$
5i (73)	173-175 dec (G)	$C_{14}H_{16}NO_2Br$
5j (56)	164-167 dec (F)	$C_{14}H_{15}NO_2Cl$
6 (73)	83-84 dec (H)	$C_{19}H_{23}NO_5$

[a] A, EtOAc-$(i\text{-Pr})_2O$; B, EtOH-H_2O; C, H_2O; D, MeOH-H_2O; E, MeOH; F, CH_2Cl_2-petroleum ether; G, $CHCl_3$-petroleum ether; H, $(i\text{-Pr})_2O$. [b] All compounds in this table for which empirical formulas are listed were analyzed for C, H, and N, and the observed values were within ±0.4% of the theoretical values. [c] Lit.[4] mp 143 °C. [d] Lit.[3c] mp 87-88 °C.

Biological Results and Discussion. The data for the in vivo antileukemic assays (P388) are listed in Table II. All of the compounds tested showed significant reproducible activity in this assay down to the lowest dose tested, 12.5 mg/kg. Activity at this dose ranged from % T/C = 190–132 for **2e** and **2c**, respectively; animal weight difference (T - C) ranged from −3.1 to −1.1 g for **2e** and **2c**, respectively. It is significant that several compounds showed activity with no toxicity over the fourfold dose range tested and two of these compounds, **2a** and **2e**, have been selected for more detailed testing against a panel of solid tumors.

All of the compounds tested in this study are quite lipophilic; calculated log *P* values range from 4.25 to 6.53 for **2c** and **2e**, respectively.[5] Clearly these compounds are considerably more lipophilic than mitomycin C[6] and several other antileukemic compounds that have been reported in the literature.[7]

The stability of diacetate **6** was studied in the NMR (aqueous Me_2SO) in an effort to compare its reactivity with the previously reported pyrrolizine diacetates.[2b] Unfortunately, the similarity of chemical shifts between the C-2

Table II. In Vivo Antileukemic Activity (P388)[a,b]

Compd	Dose,[c] mg/kg	Toxicity day survivors[d]	Animal wt diff (T − C)	% T/C
2a	50	5/5	−0.5	171
	25	6/6	−2.4	142
	12.5	6/6	−2.6	152
2b	50	5/6	−3.8	90
	25	6/6	−3.4	150
	12.5	6/6	−3.0	152
2c	50	2/6	−3.4	<50
	25	6/6	−1.6	146
	12.5	6/6	−1.1	132
2d	50	6/6	−2.6	133
	25	6/6	−2.3	136
	12.5	6/6	−2.5	142
2e	50	4/6	−4.9	65
	25	6/6	−4.1	152
	12.5	6/6	−3.1	190
2f	200[e]	0/6	−1.5	<50
	100[e]	5/6	−2.1	<50
	50[e]	6/6	−2.0	<50
	25[e]	6/6	−1.6	127
	25	6/6	−1.7	148
	12.5	5/6	−1.3	145
	6.25	5/6	−2.1	134
2g	50	6/6	−2.6	133
	25	6/6	−2.1	155
	12.5	6/6	−2.6	142
2h	50[f]	5/6	−2.9	80
	25[f]	6/6	−3.8	142
	12.5[f]	6/6	−1.3	145
2i	50	5/6	−4.9	88
	25	6/6	−3.9	142
	12.5	6/6	−2.0	152
2j	50[f]	6/6	−2.6	84
	25[f]	6/6	−2.9	148
	12.5[f]	6/6	−1.5	160
6	50	4/6	−3.2	75
	25	6/6	−3.8	95
	12.5	6/6	−1.6	157

[a] Determined under the auspices of the National Cancer Institute, National Institutes of Health. For general screening procedures and data interpretation, see R. I. Geran, N. H. Greenberg, M. M. MacDonald, A. M. Schumacher, and B. J. Abbott, *Cancer Chemother. Rep., Part 3*, 3 (2), 1 (1972). [b] Ascitic fluid containing ca. 6×10^6 cells was inoculated into male CDF_1 mice (ip route); in this assay median survival times of % T/C $\geq$ 125 are considered significant. [c] The compound was administered by the ip route in a Flucel (hydroxypropylcellulose) suspension. A total of nine daily doses was given starting 24 h after tumor inoculation. [d] Recorded on the fifth day. [e] Female CDF_1 mice were used in this assay. [f] Saline was used as the vehicle in this assay.

and C-5 methyls and the acetate methyls precluded this method of analysis. Other approaches to comparison of reactivities amenable to these two classes of compounds and other related compounds are currently being evaluated.

Work directed toward the elucidation of the mode of action of these related compounds[2b] is currently in progress. Furthermore, several additional series of compounds based upon different heterocyclic systems are currently undergoing antileukemic evaluation. The results obtained from these and additional studies in progress should afford a more clear picture of the structural requirements of these systems.

Experimental Section

Melting points (uncorrected) were determined in open capillary tubes with a Thomas-Hoover Unimelt apparatus. IR spectra were determined as KBr wafers unless otherwise specified with a Perkin-Elmer 237 spectrophotometer. NMR spectra were determined for $CDCl_3$ solutions (unless otherwise specified) containing ca. 1% Me_4Si as internal standard with a Varian T-60 spectrometer. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, Ga. Typical experimental procedures and spectral data are presented below.

***N*-Acetyl-*N*-phenylalanine (3f).** A mechanically stirred solution of *dry* acetanilide (33.79 g, 0.25 mol) in anhydrous toluene (500 mL) was treated with NaH (57% oil dispersion, 11.57 g, 0.28 mol) and heated under reflux for 2 h. Ethyl 2-bromopropionate (37.5 mL, 0.29 mol) was added and the mixture was refluxed for 2 h. The cooled mixture was centrifuged to facilitate separation of the NaBr and filtered, and the toluene solution was evaporated to dryness in vacuo. The syrupy residue was dissolved in ethanol (300 mL), a solution of NaOH (20 g) in water (30 mL) was added, and the mixture was heated under reflux for 1 h. The cooled solution was concentrated in vacuo, water (700 mL) was added, and the mixture was extracted with CH_2Cl_2 (2×200 mL). The mixture was acidified to pH 1 with concentrated HCl, the precipitate which formed was redissolved by heating, and **3f** (35.8 g, 60%) crystallized as small soft white prisms: mp 141–145 °C (lit.[4] mp 143 °C); IR 2905, 1738 ($\nu_{C=O}$), 1620, 1496, 1312, and 836 cm^{-1}; NMR δ 1.34 (d, J = 7.5 Hz, 3 H), 1.92 (s, 3 H), 5.02 (q, J = 7.5 Hz, 1 H), 7.51 (s, 5 H), and 11.47 (s, 1 H, CO_2H).

Dimethyl *N*-Phenyl-2,5-dimethylpyrrole-3,4-dicarboxylate (4f).[3c] A solution of *N*-acetyl-*N*-phenylalanine (**3f**, 20.72 g, 0.10 mol) in acetic anhydride (100 mL) and dimethyl acetylenedicarboxylate (DMAD, 50 mL, 0.40 mol) was stirred in a flask equipped with a reflux condenser and a gas bubbler to monitor CO_2 evolution during the reaction. The mixture was heated to 65 °C (bath temperature) over a 15-min period and maintained at this temperature for 1 h *after* the rate of gas evolution had substantially decreased. The mixture was concentrated to dryness in vacuo and the syrupy residue was quickly dissolved in hot methanol (ca. 200 mL), filtered, and allowed to cool to yield 25.28 g (88%) of **4f** as large colorless transparent needles: NMR δ 2.19 (s, 6 H), 3.90 (s, 6 H), and 7.17–7.80 (m, 5 H); IR ($\nu_{C=O}$) 1692 and 1715 cm^{-1}.

***N*-Phenyl-2,5-dimethyl-3,4-bis(hydroxymethyl)pyrrole (5f).** A solution of **4f** (11.49 g, 0.04 mol) in dry dichloromethane (50 mL) was added dropwise over a 15-min period to a mechanically stirred mixture of lithium aluminum hydride (3.04 g, 0.08 mol) in anhydrous ether (100 mL) heated under reflux (50–55 °C bath). The stirred mixture was heated under reflux for 1 h after the addition was complete and then cooled in an ice bath. The excess hydride was carefully decomposed with small additions of wet ether and then with water until the salts were white. The mixture was filtered (medium-porosity sintered-glass funnel) and the inorganic residue was washed with several portions of hot dichloromethane (ca. 30 mL) until the total filtrate volume was 400 mL. The filtrate was concentrated in vacuo to a volume of ca. 125 mL, warmed to boiling, and diluted with slow portionwise addition of petroleum ether (ca. 100 mL) to yield 8.592 g of **5f** (93%) as tiny colorless needles which were analytically pure: NMR δ 2.03 (s, 6 H), 3.33 (br s, 2 H), 4.66 (s, 4 H), and 7.17–7.67 (m, 5 H).

***N*-Phenyl-2,5-dimethyl-3,4-bis(hydroxymethyl)pyrrole Bis(*N*-methylcarbamate) (2f).** A cooled (ca. 10 °C) stirred solution of **5f** (2.315 g, 0.01 mol) in dichloromethane (25 mL) containing triethylamine (0.25 mL) was treated with methyl isocyanate (3.0 mL, 0.05 mol) and then heated under reflux (50 °C bath) for 2 h. The solution was cooled and concentrated to dryness in vacuo and the solid residue was dissolved in hot ethyl acetate and filtered. The filtrate was concentrated in vacuo to ca. 25 mL, heated to boiling, and carefully diluted with portionwise additions of hot isopropyl ether (ca. 75 mL) to yield, upon cooling, 3.12 g (90%) of **2f** as a very fluffy white wool: NMR δ 2.04 (s, 6 H), 2.76 (s, 3 H), 2.84 (s, 3 H), 5.10 (br s, 2 H), 5.17 (s, 4 H), and 7.10–7.67 (m, 5 H); IR ($\nu_{C=O}$) 1695 cm^{-1}.

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(5) (a) The observed log *P* for 1-phenylpyrrole is 3.08;[5b] adding π increments for the C-2 and C-5 methyl groups (1.16), the C-3 and C-4 methylene groups (1.00), the two unsubstituted carbamate residues, i.e., $OCONH_2$ (−2.10), and the two *N*-methyl groups (1.16), one finds a calculated log *P* for **2f** = 4.30.[5c] The π increment for the *n*-butyl groups is 2.13[5b] and for the methylenedioxy group, −0.05.[5c] (b) C. Hansch, S. D. Rockwell, P. Y. C. Jow, A. Leo, and E. E. Steller, *J. Med. Chem.*, **20**, 304 (1977); (c) C. Hansch, A. Leo, S. H. Unger, K. H. Kim, D. Nitaitani, and E. J. Lien, *ibid.*, **16**, 1207 (1973).
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Quinazolines and 1,4-Benzodiazepines. 81.[1] *s*-Triazolo[4,3-*a*][1,4]benzodiazepines by Oxidative Cyclization of Hydrazones

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s-Triazolo[4,3-*a*][1,4]benzodiazepines bearing various substituents in the 1 position were prepared by oxidative cyclization of the appropriate aldehyde hydrazones of 2-hydrazinobenzodiazepines. Diethyl azodicarboxylate and activated manganese dioxide were used as oxidizing agents. The new triazolo compounds were active in the CNS tests but none of them reached the potency of the known triazolobenzodiazepines.[2]

The conventional synthesis of the *s*-triazolo[4,3-*a*]-[1,4]benzodiazepines **8–10**[2] by dehydration–cyclization of the 2-(2-acylhydrazino)benzodiazepines **6** often requires vigorous reaction conditions and gives diminishing yields as the bulk of the substituent R in the 1 position increases. The steric hindrance affecting this ring closure can be avoided by employing the intermediate triazolines **7**. These triazolines should exist in equilibrium with the open hydrazones **2–5**. Once formed, the triazolines should be readily dehydrogenated to the triazoles by common oxidizing agents. A process using air as oxidant has been disclosed by Hester and Szmuszkovicz.[3]

We would like to report some of our results, in particular experiments which involved the use of diethyl azodicarboxylate or activated manganese dioxide as oxidizing agents, which led to both known and new triazolobenzodiazepines in good to excellent yields.

Thus, reaction of the known 2-hydrazinobenzodiazepines[4,5] with the appropriate aldehyde gave the corresponding hydrazones **2–5**. The spectral data of the characterized hydrazones were in agreement with the assigned structures. The NMR spectrum of **2a** in Me_2SO indicated the presence of only one form while an equilibrium of syn and anti forms was established in chloroform solution. The cyclic form **7a** was not detectable by NMR spectroscopy. When the acetaldehyde hydrazone **2a** was heated in boiling benzene in the presence of diethyl azodicarboxylate, the known triazolo compound **8a**[6] was obtained in 70% yield. Employing activated manganese dioxide in place of the azo reagent gave **8a** in about half this yield. As demonstrated for the preparation of **9a**,[4] **11d**, and **12**, it was not necessary to isolate the hydrazones prior to conversion to the triazole.

The methyl ester **10a** was obtained via the glyoxylic ester hydrazone **3a** and was reduced with PCl_3 to **10b** (Scheme I).

The dihydroxyethyl derivatives **11a,b,d** were accessible by the oxidative cyclization of the *dl*-glyceraldehyde hydrazones **4** and were of interest as possible stable, water-soluble triazolobenzodiazepines. However, their water solubility in relation to their pharmacological potency was not considered sufficient to pursue these compounds further.

Table I. Pharmacological Data for Triazolobenzodiazepines

Compd	Mouse (ED_{50}, mg/kg po)		
	Inclined screen	Footshock anti-fighting	Anti-pentyl-enetetra-zole
8a	>400	100	3.35
8b	2	2.5	0.3
9b	>400	0.5	1.1
10b	40	5	0.9
11a	>400	>100	620
11b	100	20	3.8
11d	200	5	1.5
12c	150	6.25	4.2
12d	150	2.5	1.3
13c	>400	>100	>800
14	500	50	2.8
15	300	100	50
Diazepam	25	10	1.4
Chlordiazepoxide	100	40	8

The 1-vinyl compounds **12c** and **12d** were isolated by chromatography in low yield due to the formation of polymeric by-products. The interesting adduct **13c** was isolated as a by-product and probably was formed by addition of diethyl hydrazodicarboxylate to the vinyl compound **12c**, followed by subsequent dehydrogenation to the unsaturated derivative with trans configuration. Reaction of the ester **10b** with hydrazine yielded the hydrazide **14** (Scheme II). Similarly, the basic amide **15** was obtained by heating the ester **10b** with 2-(dimethylamino)ethylamine. Hydrolysis of **10b** was accompanied by decarboxylation and afforded **9b**. The same