appears to be a combination of indole and 2-acylindole chromophores: λ_{max} (mμ) 291 (ϵ 7230), 282 (8400), 274 (8120), and 220 (39,100), λ_{sh} 310 mμ (ϵ 2020). The infrared spectrum (chloroform solution) shows carbonyl absorption at 1640 cm.$^{-1}$ and the n.m.r. spectrum exhibits a sharp signal at τ 8.06 ascribed to the N-methyl group. Dihydroburnamicine has a pK_a of 9.02 (50% methanol–water) which is very close to that reported for burnamicine.[2]

The mass spectrum of dihydroburnamicine[8] provides further confirmation for the proposed structure. The parent mass peak at m/e = 328 was also the most intense line in the spectrum. The anticipated fragmentations along lines a, b, and c are those observed for burnamicine.[2] The expected fission along a gave medium intensity peaks at m/e = 128, 129, and 130 from the indole fragment. A medium intensity peak at m/e = 170 is considered to arise by cleavage along b and by loss of carbon monoxide (mass 28) from the fragment of mass 198 formed from fission along a. The peak at m/e = 170 thus corresponds to the strong peak at m/e = 168 in the mass spectrum of burnamicine. The second strongest peak in the spectrum, m/e = 143, and a peak at m/e = 144 correspond to the intense peaks at the same m/e in the mass spectrum of burnamicine and could have arisen as previously suggested for burnamicine. The mass spectrum of dihydroburnamicine also shows a peak at m/e = 310 which corresponds to the peak at m/e = 308 in the mass spectrum of burnamicine resulting from the loss of the elements of water in both cases.[2] The synthesis of other indole alkaloids from compound II is under investigation.[9]

(8) We are indebted to Dr. Taylor for the mass spectrum and his helpful interpretation.

(9) Satisfactory analytical data were obtained for all new compounds described in this communication.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF OREGON
EUGENE, OREGON

LLOYD J. DOLBY
SHIN-ICHIRO SAKAI

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Viomycin. I. The Structure of Viomycidine

Sir:

On complete acid hydrolysis, the tuberculostatic *streptomyces* antibiotic viomycin[1] yields carbon dioxide, ammonia, urea L-serine, L-α,β-diaminopropionic acid,[1,2] L-β-lysine,[3,4] and a basic amino acid[1,2] which we have named viomycidine (I). Ion-exchange separation of viomycin hydrolysate followed by charcoal chromatography of the fraction containing strongly basic amino acids gave I as a crystalline hydrochloride, m.p. 200–208° dec., $[\alpha]^{30}D$ −78° (c 1.78, water). *Anal.* Calcd. for $C_6H_{10}O_2N_4 \cdot HCl$: C, 35.00; H, 5.36; O, 15.48; N, 27.65; Cl, 17.18. Found: C, 35.07; H, 5.31; O, 14.20; N, 27.49; Cl, 16.97. C-Methyl, O-methyl, N-methyl, and primary amino groups were shown to be absent. Viomycidine had pK_a values of 2.8, 5.87, and 13.4 (in 66% dimethylformamide) and 1.3 (estimated), 5.50, and 12.6 (in water)[5]; it gave positive Sakaguchi, Weber, and ninhydrin tests and negative Tollens, Benedict, and Benedict–Behre tests. Viomycidine hydrochloride showed strong infrared absorption at (μ) 2.98, 3.18, 3.50, 5.91, 6.06, 6.87, and 7.10, among others; it displayed only end absorption in the ultraviolet region. The n.m.r. spectrum of I-hydrochloride in deuterium oxide solution showed five nonexchangeable protons present. Absorptions were present at τ 4.37 (1H, triplet, J = 2.4 c.p.s.), 5.38 (2H, multiplet), and 7.43 (2H, triplet, J = 1.9 c.p.s.).

Guanidine was detected as a product of nitric acid oxidation of I; the strongly basic group present in I was assigned to a monosubstituted guanidine function because of the strongly positive Sakaguchi reaction. The nonguanidine nitrogen of I was characterized as an imine due to (i) its weakly basic nature, (ii) its differential ultraviolet spectrum (λ_{max} 212 mμ (ϵ 2530), pH 9.80 *vs.* 3.82),[5] characteristic of tertiary amines,[6] and (iii) a positive *o*-aminobenzaldehyde test.[7,8] I consumed 1 mole of hydrogen (platinum–acetic acid). Thus viomycidine contains a strongly acidic carboxyl group, a monosubstituted guanidine function, one reducible double bond, and, therefore, one ring. Because I is stable to vigorous acid hydrolysis, three- and four-membered rings containing nitrogen are excluded and I must contain a Δ^1-pyrroline ring.

Hydrolysis of I by hot barium hydroxide solution furnished nearly 3 moles of ammonia[10]; no other volatile base was formed. From the hydrolysate pyrrole-2-carboxylic acid[11] was isolated in 21% yield. Sodium hydroxide fusion of I gave 2-aminopyrimidine,[11,12] pyrrole-2-carboxylic acid,[11] and glycine[11,12]; no volatile base other than ammonia was formed. The products of alkaline hydrolysis of viomycidine place the carboxyl group at an α-position of the Δ^1-pyrroline nucleus.

The n.m.r. spectra of viomycidine and related compounds[13] indicate the absence of an olefinic-type proton in I.

(1) T. H. Haskell, S. A. Fusari, R. P. Frohardt, and Q. R. Bartz, *J. Am. Chem. Soc.*, **74**, 599 (1952).

(2) L. H. Mason, Ph.D. Thesis, University of Illinois, 1953.

(3) H. E. Carter, W. R. Hearn, E. M. Lansford, Jr., A. C. Page, Jr., N. P. Salzman, D. Shapiro, and W. R. Taylor, *J. Am. Chem. Soc.*, **74**, 3704 (1952).

(4) E. E. van Tamelen and E. E. Smissman, *ibid.*, **74**, 3713 (1952).

(5) We are grateful to Dr. Harold Boaz, Eli Lilly and Co., for obtaining these data.

(6) G. W. Stevenson and D. Williamson, *J. Am. Chem. Soc.*, **80**, 5943 (1958).

(7) W. B. Jakoby and J. Fredericks, *J. Biol. Chem.*, **234**, 2145 (1959).

(8) In this test, I showed λ_{max} 301 mμ. Δ^1-Pyrroline showed λ_{max} 288 mμ; 2-methyl-Δ^1-pyrroline-5-carboxylic acid[9] showed λ_{max} 296 mμ. Viomycidine and all imines and Δ^1-pyrrolines tested showed broad shoulders of low extinction in the region 420–480 mμ, responsible for the yellow color of the positive test.

(9) We are grateful to Dr. H. Gershon, Pfister Chemical Works, Inc., for a sample of this compound.

(10) Under these conditions arginine gives only 2 moles of ammonia.

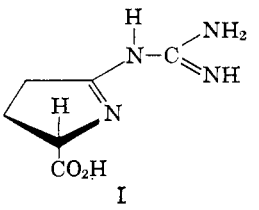
(11) Identified by comparison with an authentic sample, melting point, mixture melting point, infrared, ultraviolet, and n.m.r. spectra, color reactions, and paper chromatographic behavior. The transformation of I into this substance and the structural inferences derived therefrom will be fully developed in the complete paper.

(12) The formation of 2-aminopyrimidine and glycine on base fusion is considered to proceed through a derivative of β-guanidopropionaldehyde, derivable from I by isomerization, ring opening, and cyclization.

(13) The n.m.r. spectrum of I in trifluoroacetic acid showed absorptions at τ 4.07 (1H), 5.05 (2H), and 7.23 (2H); guanidinium absorptions were present from τ 1.5 to 3.0. The n.m.r. spectrum of Δ^1-pyrroline in trifluoroacetic acid solution showed absorptions at τ 1.20 (position 2, 1H), 6.75 (position 3, 2H), 7.58 (position 4, 2H, quintet, J = 4.0 c.p.s.), and 5.73 (position 5, 2H); no absorption was present that might be assigned to the protonated imine. The olefinic proton of isobutylideneethylamine absorbs at τ 2.47 (neat liquid) and at 1.66 (trifluoroacetic acid solution); the olefinic proton of isobutylideneazine absorbs at τ 2.32 (neat liquid); the olefinic proton of 5,5-dimethyl-Δ^1-pyrroline absorbs at τ 3.1 (neat liquid).[14]

(14) R. Bonnett and D. E. McGreer, *Can. J. Chem.*, **40**, 177 (1962).

Viomycidine was most conveniently characterized by a highly crystalline N-2,4-dinitrophenyl derivative, m.p. 171.5–172.5°. *Anal.* Calcd. for $C_{12}H_{12}O_6N_6 \cdot 2H_2O$: C, 38.71; H, 4.33; N, 22.58. Found: C, 38.71; H, 4.57; N, 23.03. On acetylation using aqueous acetic anhydride, I was converted into a crystalline N-acetyl derivative, m.p. 256–257°, $[\alpha]^{28}D$ 41.5° (*c* 2.4, water). *Anal.* Calcd. for $C_8H_{12}O_3N_4$: C, 45.28; H, 5.70; N, 26.43. Found: C, 45.41; H, 5.91; N, 26.59. The derivative gave positive Weber and Sakaguchi tests but negative ninhydrin and *o*-aminobenzaldehyde tests; it showed only end absorption in the ultraviolet region and had pK_a values of 4.86 and 13.0 (in 66% dimethylformamide).[5] Acid hydrolysis of the acetyl derivative converted it into viomycidine as the only observable product. These data suggest an N-acetyl-Δ^2-pyrroline structure[15] for acetylviomycidine. The positions of the double bond and the guanidine group of viomycidine were determined by a study of the ozonolysis products of acetylviomycidine. When acetylviomycidine was subjected to ozonolysis, oxidative work-up, and acid hydrolysis, guanidine and aspartic acid[16] were produced in good yield and as the only observable products. Thus acetylviomycidine is 1-acetyl-2-guanido-Δ^2-pyrroline-5-carboxylic acid and viomycidine (I) is 2-guanido-Δ^1-pyrroline-5-carboxylic acid.[18–20] Because viomycidine is more dextrorotatory in acid (M_D −10.3°) than in



I

water (M_D −37.6°), application of the Clough–Lutz–Jirgensons rule[21] suggests the L (or (*R*)) configuration for the asymmetric center present.

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(15) Δ^1-Pyrrolines give, on acetylation, either N-acetyl-Δ^2-pyrrolines, ring-opened N-acyl carbonyl compounds, or a mixture of the two derivatives. See, for example, F. C. Uhle and F. Sallman, *J. Am. Chem. Soc.*, **82**, 1190 (1960), and P. J. A. Demoen, P. A. J. Janssen, and J. L. M. Loomans, *ibid.*, **81**, 6286 (1959).

(16) The procedure used was similar to that of Zbiral,[17] who in this way obtained aspartic acid from Δ^1-pyrroline-5-carboxylic acid. The aspartic acid isolated was racemic, racemization apparently having occurred during treatment of I with hot pyridine–acetic anhydride.

(17) E. Zbiral, *Monatsh. Chem.*, **94**, 639 (1963).

(18) We thank Dr. E. F. Ullman for suggesting that structures similar to I would be stable to hydrolysis, and Dr. Jack Hine for valuable discussions.

(19) To our knowledge, viomycidine is the first stable compound containing an α,β-unsaturated guanidine unit. This formulation is also suggested by the differential ultraviolet spectrum shown by the guanidine group of viomycidine (pH 9.0 *vs.* pH 13.1, λ_{max} 222 mμ (ϵ 1690)).[5] Saturated alkylguanidines do not display differential ultraviolet spectra.

(20) The n.m.r. absorptions of the protons of viomycidine in deuterium oxide solution are assigned as follows: C-3(2H), τ 5.38; C-4(2H) 7.43, C-5(1H) 4.37.

(21) J. P. Greenstein, *Advan. Protein Chem.*, **9**, 121 (1954).

SCHOOL OF CHEMISTRY
GEORGIA INSTITUTE OF TECHNOLOGY
ATLANTA, GEORGIA 30332

JOHN R. DYER
H. B. HAYES
E. G. MILLER, JR.
R. F. NASSAR

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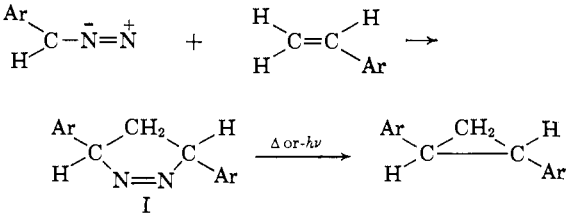
cis-3,5-Bis(*p*-Methoxyphenyl)-1-pyrazoline. A *cis–trans* Isomer Pair of Cyclic Azo Compounds

Sir:

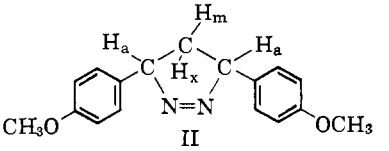
Previous communications in this series[1–3] had described the synthesis of *trans*-3,5-diaryl-1-pyrazolines (I) *via* the presumed stereospecific 1,3-dipolar addition[4] of aryldiazoalkanes to the corresponding styrenes. Evidence for their *trans*-configuration[2] and their stereospecific thermal decomposition[1,3] to the corresponding *trans*-1,2-diarylcyclopropanes was also presented.



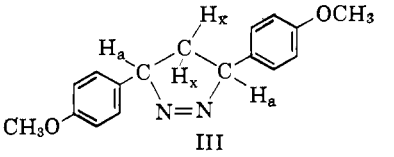
I

However, since the corresponding *cis*-1-pyrazolines were not available, no comparative study of their chemical behavior with that of the *trans* isomers could be made. We would like to report, for the first time, the isolation of a *cis*-3,5-diaryl-1-pyrazoline of type I.

As an extension of the 1-pyrazoline synthesis from aryldiazoalkanes and styrenes,[3] the reaction of *p*-methoxyphenyldiazomethane with *p*-methoxystyrene was investigated. A 36% yield of what proved to be a mixture of the *cis* and *trans* isomers of 3,5-bis(*p*-methoxyphenyl)-1-pyrazoline was obtained. The *cis–trans* ratio was estimated to be 55:45 by n.m.r. spectral analysis. By careful fractional crystallization, each isomer was separated in 95% minimum purity.



II



III

The expected *trans*-3,5-bis(*p*-methoxyphenyl)-1-pyrazoline (III) crystallized as off-white plates (from methanol), m.p. 129° dec., λ_{max}^{EtOH} 332 mμ (ϵ_{max} 533); the –N=N– bond appeared as a weak absorption at 1555 cm.$^{-1}$. The n.m.r. spectrum consisted of a quartet at τ 2.98 (aromatic protons), a triplet at 4.25 (benzylic protons), a singlet at 6.26 (methoxy protons), and a triplet at 7.95 (methylene protons). This perfect agreement with the spectral data of the other *trans*-3,5-diaryl-1-pyrazolines[2] leaves no doubt as to the *trans* configuration of the 3,5-substituents of this isomer.

cis-3,5-Bis(*p*-methoxyphenyl)-1-pyrazoline (II) was isolated as silvery plates (from methanol), m.p. 114° dec., λ_{max}^{EtOH} 329 mμ (ϵ_{max} 329); its infrared spectrum had a weak band at 1545 cm.$^{-1}$ assigned to the azo linkage. The n.m.r. spectrum was more complicated

(1) C. G. Overberger and J-P. Anselme, *J. Am. Chem. Soc.*, **84**, 869 (1962).

(2) C. G. Overberger, J-P. Anselme, and J. R. Hall, *ibid.*, **85**, 2752 (1963).

(3) C. G. Overberger and J-P. Anselme, *ibid.*, **86**, 658 (1964).

(4) R. Huisgen, *Angew. Chem.*, **75**, 604, 741 (1963).