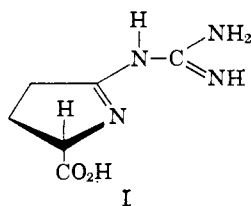


Viomycin was most conveniently characterized by a highly crystalline *N*-2,4-dinitrophenyl derivative, m.p. 171.5–172.5°. *Anal.* Calcd. for $C_{12}H_{12}O_6N_6 \cdot 2H_2O$: C, 38.71; H, 4.33; N, 22.58. Found: C, 38.71; H, 4.57; N, 23.03. On acetylation using aqueous acetic anhydride, I was converted into a crystalline *N*-acetyl derivative, m.p. 256–257°, $[\alpha]_D^{25}$ 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 viomycin as the only observable product. These data suggest an *N*-acetyl- Δ^2 -pyrroline structure¹⁵ for acetylviomycin. The positions of the double bond and the guanidine group of viomycin were determined by a study of the ozonolysis products of acetylviomycin. When acetylviomycin was subjected to ozonolysis, oxidative work-up, and acid hydrolysis, guanidine and aspartic acid¹⁶ were produced in good yield and as the only observable products. Thus acetylviomycin is 1-acetyl-2-guanido- Δ^2 -pyrroline-5-carboxylic acid and viomycin (I) is 2-guanido- Δ^1 -pyrroline-5-carboxylic acid.^{18–20} Because viomycin is more dextrorotatory in acid ($M_D -10.3^\circ$) than in



water ($M_D -37.6^\circ$), application of the Clough-Lutz-Jirgensons rule²¹ suggests the *L* (or *R*) configuration for the asymmetric center present.

Acknowledgment.—This work was supported by Research Grant E-2007 from the Institute of Allergy and Infectious Diseases of the National Institutes of Health, Public Health Service. We are grateful to Dr. L. M. Long, Parke, Davis and Co., for supplies of viomycin.

(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. Saltman, *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, viomycin 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 viomycin (pH 9.0 vs. pH 13.1, λ_{max} 222 $m\mu$ (ϵ 1690)).⁵ Saturated alkylguanidines do not display differential ultraviolet spectra.

(20) The n.m.r. absorptions of the protons of viomycin 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).

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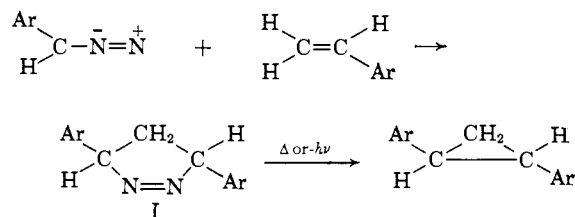
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RECEIVED OCTOBER 16, 1964

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

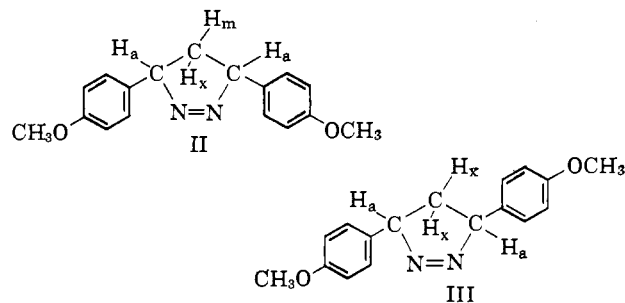
Sir:

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 addition⁴ of aryldiazoalkanes to the corresponding styrenes. Evidence for their *trans*-configuration² and their stereospecific thermal decomposition^{1,3} to the corresponding *trans*-1,2-diarylcyclopropanes was also presented.



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.



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 $m\mu$ (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-pyrazolines² 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 $m\mu$ (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).

than that of the *trans* isomer as anticipated,^{2,5} but agreed perfectly with a *cis* configuration of the 3,5-anisyl groups. Since the two methylenic protons H_m and H_x are no longer equivalent, a more complex spectrum should be observed. Indeed, while the aromatic protons appeared as a quartet centered at τ 2.92 and the methoxyl protons showed a singlet at τ 6.19, the remaining protons exhibited the splitting expected of structure II. The benzylic protons H_a appeared as a quartet at τ 4.80, being split by the nonequivalent protons H_m and H_x . Proton H_m , *trans* to the aryl groups, exhibited a sextet at a lower field than the methylene protons of the *trans* isomer (deshielded), τ 7.66 ($J_{AM} = 7.9$ c.p.s. and $J_{MX} = 12.4$ c.p.s.) compared to τ 7.95. The splitting was also in agreement with *cis* structure II, H_m being split first into a doublet by H_x , then into two triplets by the two benzylic protons H_a . The same analysis applies for H_x (*cis* to the aryl groups) which appeared as a sextet at τ 8.63 ($J_{AM} = 11.5$ c.p.s. and $J_{MX} = 12.4$ c.p.s.). The shift to higher field is undoubtedly caused by the shielding due to the 3,5-substituents.

Both *cis*- and *trans*-3,5-bis(*p*-methoxyphenyl)-1-pyrazolines were isomerized to 3,5-bis(*p*-methoxyphenyl)-2-pyrazoline⁶ (IV), isolated as its N-acetyl derivative V, m.p. 91–92.5° (identified by infrared spectrum and mixture melting point comparisons). This, along with the acid-catalyzed isomerization of both isomers to the 2-pyrazoline IV (by n.m.r. spectra), confirms the 3,5-position of the substituents. Correct combustion analyses were obtained on all new compounds reported.

The thermal and photolytic decompositions of II and III to the corresponding cyclopropanes failed to show the expected stereospecificity.^{1,2} The results are summarized in Table I.

TABLE I
DECOMPOSITIONS OF II AND III

	% of cyclopropanes ^{c,d}			
	Thermal ^a		Photolytic ^b	
	<i>cis</i>	<i>trans</i>	<i>cis</i>	<i>trans</i>
II (<i>cis</i>)	43.0	57.0	57.2	42.8
III (<i>trans</i>)	6.7	93.3	0.7	99.3

^a In toluene at 100°. ^b In THF at 13°; a second set was carried out in benzene with comparable results. Corrections were made for isomerization of the cyclopropanes⁷ under the reaction conditions. ^c In all cases quantitative yields of cyclopropanes were obtained; no olefins were found. ^d Percentages were calculated by comparison of the areas under the methoxy peaks in the n.m.r. spectra of the resulting cyclopropanes (*cis* τ 6.52; *trans* 6.39°). These values are averages of two separate decompositions and are accurate to within $\pm 1.5\%$.

Samples of the *cis*- and *trans*-1,2-bis(*p*-methoxyphenyl)cyclopropanes were obtained by the base-catalyzed decomposition of 3,5-bis(*p*-methoxyphenyl)-2-pyrazoline (III), a reaction that had previously been reported to produce only the *trans* isomer.⁹

(5) J.-P. Anselme, Ph.D. Thesis, Polytechnic Institute of Brooklyn, 1964, p. 13.

(6) Prepared from the chalcone and hydrazine.

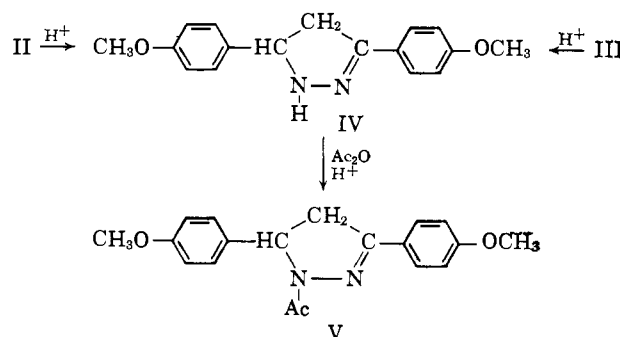
(7) There have been several recent reports concerning the photolytic isomerization of cyclopropanes in solution: G. W. Griffins, E. J. O'Connell, and H. A. Hammond, *J. Am. Chem. Soc.*, **85**, 1001 (1963); W. von E. Doering and M. Jones, Jr., *Tetrahedron Letters*, No. 12, 791 (1963); R. C. Cookson, M. J. Nye, and G. Subrahmanyam, *Proc. Chem. Soc.*, 144, 1964; G. S. Hammond, P. Wyatt, C. D. DeBeor, and N. J. Turro, *J. Am. Chem. Soc.*, **86**, 2532 (1964).

(8) Relative to TMS at 60 Mc. in Spectrograde CCl₄.

(9) M. Hamada, *Botyu-Kagaku*, **21**, 22 (1956).

Assignment of structure was made by comparison of the n.m.r. spectra with those of other *cis*- and *trans*-1,2-diarylcyclopropanes.^{2,10}

While a small increase in stereospecificity was observed in the photolytic decompositions, the *cis*-1-pyrazoline gave a considerable amount of *trans*-cyclopropane V. It is apparent from these results



that, in the biradical generated from the *cis*-1-pyrazoline (both thermally and photolytically), rotation around a single bond is faster than coupling. This may be due to steric or electronic factors or a combination thereof. Further work directed to shed some light on this question is in progress. Mechanistic considerations and details of these and other studies will be the subject of a future publication.

(10) D. Y. Curtin, et al., *J. Am. Chem. Soc.*, **83**, 4838 (1961).

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Formation of Perhydrophenalenes and Polyalkyladamantanes by Isomerization of Tricyclic Perhydroaromatics

Sir:

Adamantane¹ and its methyl and dimethyl² homologs have been prepared by aluminum halide catalyzed isomerizations of tricyclic saturated hydrocarbons having from 10 to 12 carbon atoms. In each case, two of the rings in the saturated hydrocarbon consisted of the [2.2.1]bicycloheptyl or the [2.2.2]bicyclooctyl systems and it has been assumed that these strained moieties are required for the conversions to adamantanes. We have recently found that polymethyladamantanes are formed in good yields as end products in the aluminum halide catalyzed isomerizations of perhydrogenated (Raney nickel) acenaphthene, fluorene, anthracene, and phenanthrene.³ This communication deals with the characterization and identification of a number of intermediate as well as final products of isomerization.

The mixture of at least four isomeric perhydroacenaphthenes (by v.p.c.) rapidly and exothermically formed 1-ethyladamantane in high yield on treatment with aluminum bromide-olefin complex at 0°; continued reaction at 25° resulted in an almost quantitative yield of 1,3-dimethyladamantane. 1-Ethyladamantane, b.p. 219°, m.p. -60°, n_D^{20} 1.4931,

(1) P. Schleyer and M. M. Donaldson, *J. Am. Chem. Soc.*, **82**, 4645 (1960).

(2) P. Schleyer and R. D. Nicholas, *Tetrahedron Letters*, **9**, 305 (1961).

(3) U. S. Patent 3,128,316.