ACTIDIONE, AN ANTIBIOTIC FROM STREPTOMYCES GRISEUS

Sir:

It has been found in this Laboratory that streptomycin-producing strains of *Streptomyces griseus* produce a second antibiotic which has little or no activity against bacteria but is very effective against many yeasts. The crude product was isolated from streptomycin beers by adsorbing on carbon, eluting with 80% acetone, distilling the acetone and extracting the remaining aqueous solution with chloroform. The chloroform extract was decolorized with carbon and evaporated. After purification of this crude product by counter-current distribution between benzene and water,[1] it was obtained in crystalline form. Several recrystallizations from amyl acetate yielded colorless plates, m.p. 115–116.5°, $[\alpha]^{25}D$ −2.8° (*c* 9.6, methanol). Analytical data are in good agreement with the formula $C_{27}H_{42}N_2O_7$ (mol. wt. 507). The molecular weight (cryoscopic in benzene) varied from 420 to 875, depending upon the concentration.

TABLE I

	M. p., °C.	$\alpha^{25}D$ Deg.	c^a	Formula	Percentage composition C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
Actidione	115–116.5	−2.8	9.6	$C_{27}H_{42}N_2O_7$	64.01	63.74	8.36	8.35	5.53	5.44
Diacetate	143–145	+24.6	3.7	$C_{31}H_{46}N_2O_9$	63.03	62.98	7.85	7.89	4.74	4.70
Dioxime	203–204	....	...	$C_{27}H_{44}N_4O_7$	60.42	60.66	8.27	8.29	10.44	9.85
Disemicarbazone	176–178	....	...	$C_{29}H_{48}N_8O_7$	56.12	55.53	7.79	7.70	18.05	17.71

[a] In methanol.

Treatment of the compound with acetic anhydride and sodium acetate at room temperature produced a biologically inactive diacetate, m.p. 143–145°, $[\alpha]^{25}D$ +24.6° (*c* 3.7, methanol). The dioxime melted at 203–204° and the disemicarbazone at 176–178°. We suggest that this compound be named *actidione* since it appears to be a diketone and is produced by an actinomycete.

Actidione is rapidly inactivated by dilute alkali at room temperature with the formation of a fragrant, dextrorotatory, volatile ketone; semicarbazone, m.p. 190–193°. Refluxing with dilute sulfuric acid does not produce the volatile ketone, but when the hydrolysate is made strongly alkaline a low molecular weight amine is evolved. Further degradation studies are now in progress.

An antibiotic spectrum of crystalline actidione was found to be very similar to that previously reported for crude preparations.[2] When tested against twelve representative bacteria it failed to inhibit at concentrations up to 1 mg. per ml. Crystalline actidione inhibits the fungal pathogen, *Cryptococcus neoformans*, in concentrations as low as 0.0002 mg. per ml. This high order of activity suggests its possible usefulness in the treatment of cryptococcosis, a rare but usually fatal disease. Toxicity tests, intravenously in mice, indicate an LD_{50} of approximately 150 mg. per kg.

Actidione has been assayed satisfactorily in concentrations as low as 0.001 mg. per ml. by an adaptation of the paper-disk plate method for streptomycin[3] using *Saccharomyces pastorianus* ATCC 2366 as the test organism.

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(1) Craig, Golumbic, Mighton and Titus, *J. Biol. Chem.*, **161**, 321 (1945).

(2) Whiffen, Bohonos and Emerson, *J. Bact.*, **52**, 610 (1946).

(3) Loo, Skell, Thornberry, Ehrlich, McGuire, Savage and Sylvester, *ibid.*, **50**, 701 (1945).

RESEARCH LABORATORIES
THE UPJOHN COMPANY
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RECEIVED JANUARY 17, 1947

THE POSSIBILITY OF FREE ROTATION IN THE SILICONES

Sir:

The low boiling points and small temperature coefficients of viscosity of the silicones have led to the view that siloxane bonds result in low cohesive forces.[1a,b] We have been determining the crystal structure of octamethylspiro[5.5]pentasiloxane[2] to see whether structural considerations would shed some light on this anomalous behavior.

Oxygen would be expected to form covalent *p* bonds at 90°. The Si–O–Si bond angle should be increased somewhat by repulsion resulting from the ionic character of the SiO bond. However, Sauer and Mead[3] calculate from the dipole moment of hexamethyldisiloxane an angle of 160 ± 15° and Frevel and Hunter[4] report a planar ring for the cyclic trimer $[(CH_3)_2SiO]_3$.

The spirosiloxane compound crystallizes with the space group $D_{4h}^{19}(I\frac{4}{a}md)$. There are four molecules in the unit cell, each molecule consisting of two planar six-membered rings linked at 90° through a common Si atom. The SiO distance is about 1.64 Å., comparable to distances found in the inorganic silicates and considerably less than the value 1.83 Å. obtained from the covalent radius sum for Si and O. The Si–C distance is 1.90 Å., the expected covalent sum.

Despite reasonable agreement between calculated and observed F^2 values for reflections with low *hkl* indices, it proved impossible to refine parameters by conventional Fourier methods. Electron density projections and sections indi-

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(1) (a) Hunter, Warrick, Hyde and Currie, THIS JOURNAL, **68**, 2284 (1946); (b) D. F. Wilcock, *ibid.*, **68**, 691 (1946).

(2) D. W. Scott, *ibid.*, **68**, 356 (1946).

(3) Sauer and Mead, *ibid.*, **68**, 1794 (1946).

(4) Frevel and Hunter, *ibid.*, **67**, 2275 (1945).

cated the methyl group was sweeping out a large umbrella-like surface, as though oscillating with a large amplitude at a fixed radius. This concept was introduced into the calculations by assuming the contribution of each methyl group to result from a precession about its equilibrium position. Important discrepancies between calculated and observed F^2 values immediately were resolved, and parameters now are being successfully refined. Because of steric reasons, two methyl groups attached to the same silicon atom could not oscillate independently over such a large area, so this is tantamount to assuming the Si atom is free to move in the ring, as in a ball and socket joint.

We consider this evidence for the extreme ionic nature of bonds in the silicone compounds. Bonds may form in the average covalent directions, but there is little resistance to angular deformation. The effect was observed only for methyl groups, probably because movement of the . . .Si–O–Si. . . atoms is constrained by the ring structure. The "softness" of the bond angles, plus the favorable geometry reducing steric interactions of attached groups, should result in a negligible barrier to free rotation about the Si–O bonds in the linear polymers. Consequently, the low boiling points and temperature coefficients of viscosity may be attributed to free rotation preventing chains from packing sufficiently closely for the short range intermolecular forces to be strongly operative.

The details of the structure analysis of the spirosilicone will be published in the near future.

RESEARCH LABORATORY
GENERAL ELECTRIC COMPANY
SCHENECTADY, NEW YORK WALTER L. ROTH
RECEIVED JANUARY 20, 1947

HYDROGENATION OF SPIROPENTANE

Sir:

The assignment of the spiropentane structure to a C_5H_8 hydrocarbon prepared by Murray and Stevenson[1] was shown to be justified by Raman spectrographic[1] and electron diffraction[2] studies. The same hydrocarbon was prepared at this Laboratory[3] by a modification of the procedure reported by Murray and Stevenson, and an identification of the structure by analysis of hydrogenation products has now been attempted.

The hydrocarbon was found to hydrogenate readily in hydrogen at 2 to 3 atmospheres in the presence of PtO_2 at room temperature. The products of the hydrogenation were separated by fractionation through a 14-mm. glass column, 7-ft. in length, packed with $^1/_8$-inch single-turn glass helices, and identified by their physical constants as indicated in the following table:

Compound	B. p., °C. Lit.[4]	B. p., °C. Found	$n^{20}D$ Lit.[4]	$n^{20}D$ Found	Moles of product
Neopentane	9.45	8–10	1.3472[a]	1.3483[a]	0.082
1,1-Dimethylcyclopropane	19.9	18–20	1.3659	1.3677[b]	.188
Isopentane	27.89	26–28	1.3539	1.3548	.043

[a] 5°. [b] 17.5°.

Infrared spectroscopic examination supported the identification proposed from the physical constants (thanks are due Dr. A. P. Cleaves of this Laboratory).

An examination of the structures of the products indicates that the strained rings of spiropentane are cleaved by hydrogen preferentially between the methylene groups. Spiro[2,5]octane has been shown to cleave in an analogous manner to yield 1,1-dimethylcyclohexane.[5]

Ethylcyclopropane and *n*-pentane, which might be expected to be among the hydrogenation products, were not found.

A detailed examination of the hydrogenation products of spiropentane by precise fractional distillation and infrared techniques will be reported later.

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(1) Murray and Stevenson, THIS JOURNAL, **66**, 812–816 (1944).

(2) Donohue, Humphrey and Schomaker, *ibid.*, **67**, 332–335 (1945).

(3) Slabey *ibid.*, **68**, 1335 (1946).

(4) Doss, "Physical Constants of the Principal Hydrocarbons," 4th ed., The Texas Company, New York, N. Y., 1943.

(5) Boord and Craig, Division of Organic Chemistry, Atlantic City Meeting, American Chemical Society, April, 1946.

AIRCRAFT ENGINE RESEARCH LABORATORY
NATIONAL ADVISORY COMMITTEE FOR AERONAUTICS
CLEVELAND, OHIO VERNON A. SLABEY
RECEIVED SEPTEMBER 12, 1946

PROPERTIES OF *m*-NITROCINNAMYL ALCOHOL

Sir:

Recently it was of some interest in this Laboratory to prepare some *m*-nitrocinnamyl alcohol. The physical properties observed for this preparation were not in accord with those previously reported in the literature, and it seems desirable to report the discrepancy.

Meerwein, *et al.* (*J. prakt. Chem.*, **147**, 211 (1936)) prepared *m*-nitrocinnamyl alcohol by the aluminum ethoxide reduction of *m*-nitrocinnamaldehyde, the product being described as light yellow needles, m. p. 51–51.5°. Effecting the reduction with aluminum isopropoxide, we obtained the material, after several recrystallizations from a 20:80 mixture of ethyl acetate and 68° ligroin, in the form of practically white needles having a pale greenish tint, m. p. 54.5°. In view of the discrepancy in melting point, the *n*-phenyl carbonate was prepared, m. p. 130°. *Anal.* Calcd.: N, 9.40. Found: N, 9.54.

UNIVERSITY OF CHICAGO
CHICAGO, ILL. ROBERT H. SNYDER
RECEIVED JANUARY 17, 1947