173° was obtained. The elementary analysis indicated that it was an acetate of 3-hydroxy-4-pteridinone.

Anal. Calcd. for $C_8H_6N_4O_3$: C, 46.6; H, 2.93; N, 27.2. Found: C, 46.5; H, 2.93; N, 27.2.

Acknowledgment.—We wish to express our gratitude to Mr. O. Sundberg and his associates for the microanalyses and to Mr. J. Morath for the photometric data.

BOUND BROOK LABORATORIES
RESEARCH DIVISION
AMERICAN CYANAMID COMPANY
BOUND BROOK, NEW JERSEY

COMMUNICATIONS TO THE EDITOR

THE STRUCTON NUMBER RULE

Sir:

A theory according to which many properties of solids and liquids can be related to the numbers and properties of the "structons" present, recently has been outlined.[1] A "structon" is defined as an atom or ion or molecule or group of atoms of a given kind, surrounded in a specified manner. A "structon number rule," relating the minimum number of structon types (S) to the number of degrees of composition freedom (F), was presented.

Application was made specifically to sodium silicate glasses. When the theory is extended to other systems, including liquid solutions, it appears advisable to express the structon number rule somewhat differently. One can still use the same equation, but now C denotes the number of types of contact between unlike structon centers. In the Na_2O–SiO_2 system, C is two, there being only Na–O and Si–O contacts. In a solution composed of two molecular species, forming strong contacts with each other (*e.g.*, by hydrogen-bonding), C is one, regardless of whether or not *like* molecules also form strong contacts.

$$S = C + F + 2 \qquad (1)$$

To determine the number of each of S types of structons requires S equations. For each of the C types of contact between different types of structon centers (A, B), there is one equation, equating the number of contacts between A-type structon centers and B neighbors to the number of contacts between B-type structon centers and A neighbors. Thus, in the high-silica region of the sodium silicate system

$$2N_{O(2Si)} + 2N_{O(2Si,Na)} + N_{O(Si,3Na)} = 4N_{Si(4O)} \qquad (2)$$

$$N_{O(2Si,Na)} + 3N_{O(Si,3Na)} = 6N_{Na(6O)} \qquad (3)$$

There is one normalizing equation. In the sodium silicate example, it expressed the fact that the total number of oxygen-centered structons equals unity (since the quantity of glass being considered was that containing a single atom of oxygen)

$$N_{O(2Si)} + N_{O(2Si,Na)} + N_{O(Si,3Na)} = 1 \qquad (4)$$

In molecular solutions, the normalizing equation may show that the sum of the mole fractions equals unity.

There is also another equation, in many cases, expressing the over-all neutrality or valence-balancing requirement; *e.g.*

$$N_{Na(6O)} + 4N_{Si(4O)} = 2[N_{O(2Si)} + N_{O(2Si,Na)} + N_{O(Si,3Na)}] \qquad (5)$$

The number of degrees of composition freedom gives the number of additional equations required to fix the numbers of all structons present. This, with the other relationships just given, leads to eq. (1).

In molecular solutions, the neutrality equation is no longer of use, hence eq. (1) must be replaced by

$$S = C + F + 1 \qquad (6)$$

This is also the equation to use if all the structon charges (see ref. 1) are zero, since then the neutrality equation is not independent; it can be obtained by appropriate addition of the structon-contact equations, such as eqs. (2) and (3). This applies, for example, to pure silica.

Application of structon theory and the structon number rule to molecular solutions will be made in another paper.

RESEARCH LABORATORIES
EASTMAN KODAK COMPANY
ROCHESTER 4, NEW YORK
MAURICE L. HUGGINS

RECEIVED JUNE 7, 1955

---

[1] M. L. Huggins, *J. Phys. Chem.*, **58**, 1141 (1954).

A CARCINOGENIC OXIDATION PRODUCT OF CHOLESTEROL

Sir:

The observation[1] that a crude progesterone preparation prepared[2] by permanganate oxidation of cholesterol dibromide and debromination produced tumors in 32% of the mice tested initiated an extended investigation in which various products of oxidation of cholesterol have been prepared in Cambridge and tested for carcinogenicity in Santa Barbara. Some of the compounds submitted for assay were suggested by specific hypotheses (an abnormal cholesteryl ester,[3] an epoxide derived from a 7,8,-9,11-diene,[4] Δ^5-cholestene-3-one[4]), others were empirically observed known or new[5] products of

---

[1] F. Bischoff and J. J. Rupp, *Cancer Research*, **6**, 403 (1946).

[2] M. A. Spielman and R. K. Meyer, THIS JOURNAL, **61**, 893 (1939).

[3] L. F. Fieser and W. P. Schneider, *ibid.*, **74**, 2254 (1952).

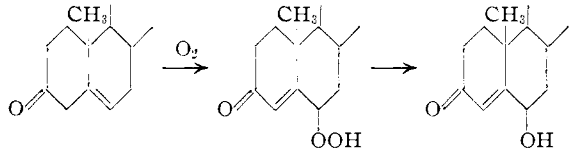
[4] L. F. Fieser, *Bull. soc. chim.*, **21**, 541 (1954); *Science*, **119**, 3099 (1954).

[5] L. F. Fieser, THIS JOURNAL, **75**, 4377, 4386, 4395 (1953).

oxidation of cholesterol. None of the products administered as aqueous colloids have had a carcinogenic effect, although a number of them administered in sesame oil have produced positive results, indicating that the presence of sesame oil is an essential link in the carcinogenic chain.[6] As recently reported,[7] cholesterol α-oxide, Δ^4-cholestene-3,6-dione, and the 1:1 complex[5] of 6β-hydroxy-Δ^4-cholestene-3-one and epicholesterol when injected into mice in sesame oil produced fibrosarcomas in 19–43% of the mice at the average age of 13–14 months. These compounds produced negative results when administered as aqueous colloids.

We wish now to report discovery of a still more potently carcinogenic oxidation product. Δ^5-Cholestene-3-one, an easily isomerized and highly reactive substance that is oxidized by lead tetraacetate to the 4α-acetoxy derivative,[8] combines with molecular oxygen in hexane solution at 25° to give a compound that crystallizes from methanol in needles, m.p. 180°, λ^{EtOH} 236 mμ (E = 16,850).

Anal. Calcd. for $C_{27}H_{44}O_3$ (416.62): C, 77.83: H, 10.65. Found: C, 77.82: H, 10.72. The substance gives an immediate color with sodium iodide–acetic acid (thiosulfate titer: mol. wt. 425) and is reduced to 6β-hydroxy-Δ^4-cholestene-3-one (III), m.p. 193°, α_D + 27.2° Chf, mixed m.p. 193–194°. Since the ultraviolet absorption corresponds to that of III, and since reduction of hydroperoxides is known to cleave the oxygen–oxygen bond, the substance is identified as 6β-hydroperoxy-Δ^4-cholestene-3-one (II).



I II III

The hydroperoxide II was given in three spaced subcutaneous injections of 5 mg. each in sesame oil to each of 32 Marsh-Buffalo mice.[9] At the age of 12 months, fibrosarcomas have appeared at the site of injection in 13 of the mice treated (average tumor age 9.6 mo.), and 17 of the remaining mice were still alive. No fibrosarcomas were observed in litter-mates given the same amount of II in aqueous colloidal solution, nor in a series of controls (up to 18 months of age) which received only sesame oil.

Indirect evidence that the precursor I can be formed from cholesterol in the body is afforded by isolation of probable transformation products: Δ^4-cholestene-3-one,[10] $\Delta^{4,6}$-cholestadiene-3-one[11] (swine spleen, arteriosclerotic aorta), and coprostanone[12] (ambergris). The possibility that antioxidants may increase resistance to spontaneous carcinogenesis is under investigation.

CHEMICAL LABORATORY OF HARVARD UNIVERSITY, CAMBRIDGE, MASS. LOUIS F. FIESER
THEODORA W. GREENE
SANTA BARBARA COTTAGE HOSPITAL RESEARCH INSTITUTE, SANTA BARBARA, CALIFORNIA
FRITZ BISCHOFF
GUILLERMO LOPEZ
J. J. RUPP

RECEIVED JUNE 24, 1955

---

[6] F. Bischoff, G. Lopez and J. J. Rupp, Abst. Am. Chem. Soc., March 3-C (1954).

[7] F. Bischoff, G. Lopez, J. J. Rupp and C. L. Gray, *Federation Proc.*, **14**, 183 (1955).

[8] L. F. Fieser and R. Stevenson, THIS JOURNAL, **76**, 1728 (1954).

[9] Supported in part by grant C 1586 C from the National Cancer Institute, National Institutes of Health, PHS.

[10] V. Prelog, *et al.*, *Helv. Chim. Acta*, **30**, 1080 (1947).

[11] E. Hardegger, L. Ruzicka and E. Tagmann, *ibid.*, **26**, 2205 (1943).

[12] E. Lederer, *et al.*, *ibid.*, **29**, 1354 (1946).

POLARIZATION OF THE 1850 Å. BAND OF AMIDES[1]

Sir:

We have recently carried out a measurement of the direction of the transition moment vector for the first N,V transition in amides.[2] Observations were made on sublimation flakes of myristamide[3] ($C_{13}H_{27}CONH_2$) with light polarized along the a and b crystallographic axes, which are also the principal directions, in the region between 2300 and 1600 Å. The orientation of samples in these experiments was obtained crystallographically with the aid of X-ray precession photographs. The ratio of the optical densities observed along the principal directions over the long-wave-length one-third of the main band was found to be constant at D_a/D_b = 14.62. This gives for the orientation of the electric moment $\theta = \pm$ arctan 0.262 where θ is measured from the a axis. The two orientations referred to the amide group itself were computed from the known crystal structure of myristamide[3] and are 9.1° and 26.7° from the line joining the nitrogen and oxygen (see Fig. 1).

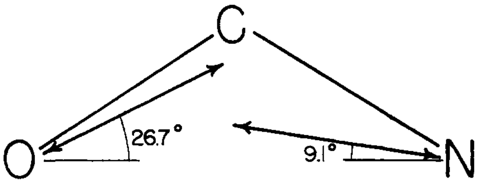


Fig. 1.—Possible orientations of the electric vector for the 1850 Å. electronic absorption band in amides.

Neither of these values agrees with conclusions from a recent experiment[4] in which absorption at 2100 Å. was found to occur essentially along one of the principal directions (also here the c crystallographic axis) of crystalline N-acetylglycine. In that work it was inferred that absorption must be nearly along the carbon–nitrogen line of the amide group, a line which is only four degrees from one of the principal directions. Possibly what was actually measured was mainly a single allowed crystal transition occupying a small region at the extreme long-wave-length edge of the main absorption. Such absorption would have to be along one or the other principal direction. Indeed we have found absorption in the region from 2120 to 2250 Å. at the long-wave-length edge of the band for myristamide which is, within experimental error, exactly along the a axis, a principal direction. In addition, we

---

[1] Supported in part by the Air Research and Development Command, Contract No. AF 18(600)-375.

[2] J. S. Ham and J. R. Platt, *J. Chem. Phys.*, **20**, 335 (1952); and H. D. Hunt and W. T. Simpson, THIS JOURNAL, **75**, 4540 (1953).

[3] The crystal structure of myristamide was determined by J. D. Turner, Ph.D. Thesis, University of Washington, 1953, and refined by R. F. Adamsky, private communication.

[4] J. C. Ward, *Proc. Roy. Soc.* (*London*), **A228**, 205 (1955).