Figure 1.

extremely disagreeable liquid blistering agent which dimerizes spontaneously in aqueous solution to yield crystalline anemonin (III or IV). The latter possesses no vesicant properties. Anemonin was first isolated in 1792 by Heyer.[2] Asahina[3,4] established that proto-anemonin (II) is the lactone of γ-hydroxyvinylacrylic acid. This was based upon synthesis of II and demonstration that the synthetic material underwent dimerization to yield anemonin. Of the numerous conceivable cyclodimerization products, Asahina proposed that anemonin possessed the 1,2-dihydroxy-1,2-cyclobutanediacrylic acid dilactone structure.
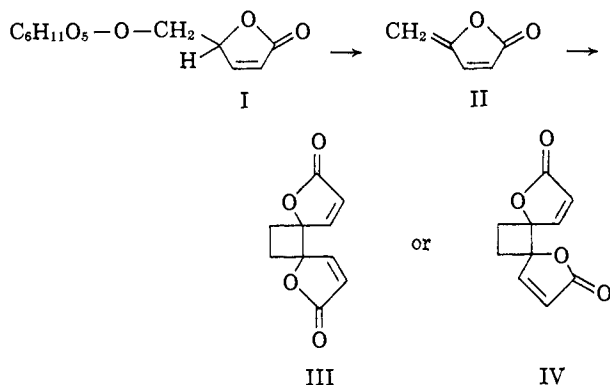
Anemonin has never been related by chemical methods to a cyclobutane derivative of known structure. The stereochemistry of the dilactone rings has been assumed to be cis (III); this conclusion has also been deduced from chemical evidence.[5] While the "head-to-head" dimeric structure appeared fairly certain, the evidence for the stereochemical relationship of the dilactone rings was rather unconvincing.[5]

The fact that only one cyclodimer is formed from protoanemonin (II) is remarkable in that at least 12 cyclobutane structures are possible for various combinations of the monomer. This large degree of stereoselectivity provoked our interest in the structure of anemonin, particularly in that the structure has especial pertinence in the more general problem of thermal cyclodimerization reactions of olefins.[6] Therefore a crystal of anemonin[7] was investigated by X-ray diffraction in order to determine the structure of the molecule, in particular the stereoconfiguration of the lactone rings.

Anemonin crystallizes in the orthorhombic system, space group Pbca, with cell dimensions $a = 11.65 \pm 0.02$ Å., $b = 13.86 \pm 0.03$ Å., and $c = 11.07 \pm 0.02$ Å., and 8 molecules in the unit cell. The computed and observed densities are 1.418 and 1.428 g./cm.^{3},

(2) M. Heyer, Chemisch Journ. V. Crell, 2, 102 (1792); A. D. Wurtz, "Dictionnaire de Chemie," Vol. I, Librarie Hackette et C, Paris, 1870, p. 299.

(3) Y. Asahina and A. Fujita, J. Pharm. Soc. Japan, 455, 1 (1920); Chem. Abstr., 14, 1384 (1920).

(4) For a discussion of the chemical transformations of anemonin see R. A. Raphael in Chemistry of Carbon Compounds, Vol. IIa, E. H. Rodd, Ed., Elsevier Publishing Co., Amsterdam, 1953, pp. 67–70.

(5) J. E. Harris, Dissertation Abstr., 20, 887 (1959).

(6) J. D. Roberts and C. M. Sharts, Org. Reactions, 12, 2 (1962).

(7) E. Shaw, J. Am. Chem. Soc., 68, 2510 (1946).

respectively. Three-dimensional intensity data were collected using the equi-inclination Weissenberg technique with Ni-filtered Cu radiation. The crystal structure was solved by obtaining phases directly from the structure factor magnitudes by the use of the symbolic addition procedure.[8] All the hydrogen atoms were located from a difference map. A least-squares refinement of the coordinates and anisotropic thermal factors using 1436 data resulted in an R factor of 13.0%.

The crystal structure determination shows that the molecule is in the trans configuration (IV, Figure 1). It also shows that the cyclobutane ring is not planar but assumes a bent configuration

with a dihedral angle of 152°. The C–C bond lengths in the cyclobutane ring range from 1.530 to 1.545 Å., a normal range for single bonds.

Selective formation of the 1,2-disubstituted adduct probably results from the stability of diradical V. This head-to-head attachment allows for the maximum delocalization of the two unpaired electrons with the adjacent unsaturated groups. The trans relationship of the two lactone rings may be rationalized on the basis of lowered destabilizing dipolar interactions in

V
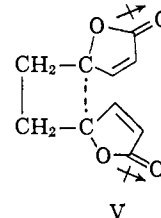
the transition state for its formation.

In the transition state for ring closure to yield the cis dilactone, the two polar lactone groups are adjacent to each other and also are pointed in the same direction. One would expect this arrangement to be less stable relative to the trans conformation because of the electronic instability associated with the proximity of the polar groups. In the trans case the lactone dipoles are opposed and the destabilizing dipolar interaction is minimized.

(8) I. L. Karle and J. Karle, Acta Cryst., 16, 969 (1963).

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The Estimation of the Angle of Twist for a Cyclobutane Derivative by Nuclear Magnetic Resonance

Sir:

In a preceding communication[1] the 1,1,2,2,-substituted cyclobutane ring of anemonin is reported to be puckered. The angle of twist, α, about the twofold axis C_2 (Figure 1) is calculated from the X-ray data to be $9.9 \pm 0.3°$. In this communication we wish to report that the angle of twist, α, can also be estimated

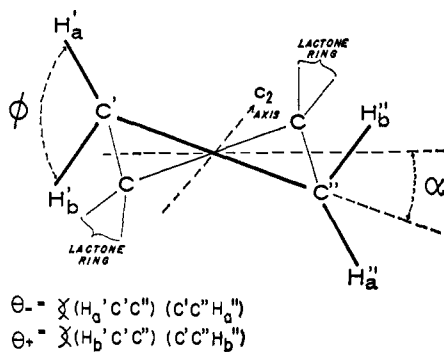(1) R. M. Moriarty, C. R. Romain, I. L. Karle, and J. Karle, J. Am. Chem. Soc., 87, 3251 (1965).

$\Theta_- = \chi(H_a'\,C'C'')\ (C'C''H_a'')$

$\Theta_+ = \chi(H_b'\,C'C'')\ (C'C''H_b'')$

Figure 1.

independently from the n.m.r. spectrum of the cyclobutane ring protons of anemonin.

As expected, an A_2B_2 type spectrum was observed for the $-CH_2-CH_2-$ portion of the cyclobutane ring (Figure 2). This pattern requires the presence of two-fold symmetry. The parameters of the spectrum are: $\delta = 0.1716$ p.p.m., $J_a = 10.72$ c.p.s., $J_b = 2.24$ c.p.s., $J_1 = 10.19$ c.p.s., and $J_2 = -12.15$ c.p.s. J_a and J_b are coupling constants between equivalent protons and J_1 and J_2 are coupling constants between nonequivalent protons. J_a and J_b will then be either the two vicinal cis coupling constants in the case of the cis isomer, or the two trans coupling constants in the case of the trans isomer. Vicinal coupling constants are a function of dihedral angles.[2] In the cis compound where the members of each pair of equivalent protons are very nearly eclipsed ($\vartheta_a \approx \vartheta_b \approx 0$), J_a and J_b will be of similar magnitude, but in a trans compound, where the dihedral angles ϑ_+ and ϑ_- (Figure 1) need not be equal, J_a and J_b, which are now trans coupling constants, can be quite different. In fact, in the present case they differ by about 8 c.p.s.; a difference of this magnitude has not been reported as yet for vicinal proton coupling constants in cyclobutanes.

This immediately suggested a trans configuration for anemonin, as indeed was found to be the case.[1] Furthermore, a comparison of the two trans coupling constants J_a and J_b allows one to estimate the angle of twist, α, of the cyclobutane ring. For this purpose we assume that the cyclobutane ring is very nearly a (twisted) square, which is borne out by the X-ray data,[3] and that the $H_a'C'H_b'$ and the $H_a''C''H_b''$ planes bisect the $CC'C''$ and $CC''C'$ angles, respectively; that is, that C_{2v} symmetry prevails about the carbon atoms C' and C''. Then the two dihedral angles ϑ_+ and ϑ_- can be related with the $H_a'C'H_b'$ and $H_a''C''H_b''$ angle and the angle of twist by

$$\cos \vartheta_\pm = \frac{\frac{1}{2} - \tan^2\left(\frac{1}{2}\varphi \pm \alpha\right)}{\frac{1}{2} + \tan^2\left(\frac{1}{2}\varphi \pm \alpha\right)}$$

A simplified Karplus relation $J = A \cos^2 \vartheta$ can now be used to estimate the angle of twist for a reasonable range of φ values between 110 and $114°$ (also suggested by the X-ray data[3]). The inherent uncertainty of A is eliminated by using the ratio of J_a and J_b. This procedure is justified because we are dealing with dihedral angles in the same molecule which both lie between 90 and $180°$.

(2) M. Karplus, J. Chem. Phys., 30, 11 (1959); cf. also M. Karplus, J. Am. Chem. Soc., 85, 2870 (1963), and references therein.
(3) I. L. Karle and J. Karle, private communication.

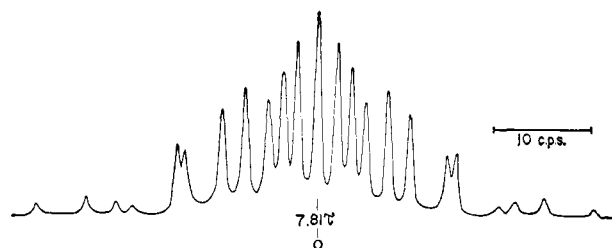Figure 2. N.m.r. spectrum (100 Mc.) of $-CH_2-CH_2-$ protons of anemonin (concentrated CH_2Cl_2 solution).

From the above considerations we estimate the angle of twist to be between 9 and $11°$. This is in excellent agreement with the figure of $9.9 \pm 0.3°$ derived from X-ray data.[3] Encouraged by this agreement, we are investigating similar cyclobutane systems in order to test the general validity of this method.

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Cyclobutadiene

Sir:

Although diene–iron tricarbonyl complexes are usually thermally stable and relatively inert chemically, nonetheless they can be readily decomposed at low temperatures, with liberation of the free diene, upon treatment with such oxidizing agents as ferric or ceric ions. We have previously taken advantage of this feature for the preparation of dienes not readily available by more standard procedures.[1] The purpose of this note is to present evidence that this same reaction sequence allows for the preparation of cyclobutadiene.[2]

Initial studies showed that cyclobutadieneiron tricarbonyl (I) decomposed in the presence of ceric ions to give, together with other materials, a dimer of cyclobutadiene.[3] It has now been shown that, when conducted in the presence of acetylenic compounds, the

I   II
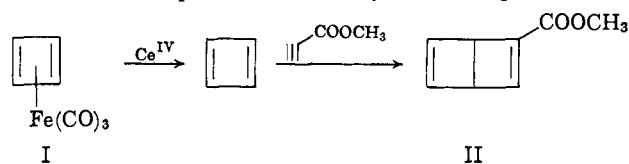
(1) J. D. Holmes and R. Pettit, J. Am. Chem. Soc., 85, 2531 (1963); D. H. Gibson and R. Pettit, ibid., 87, 2620 (1965).
(2) For leading reference to recent attempts to prepare cyclobutadiene see M. A. Avram, I. G. Dinulescu, E. Marica, G. Mateescu, E. Sliam, and C. D. Nenitzescu, Ber., 97, 382 (1964). Reference to the pertinent earlier work is given by E. Vogel, Angew. Chem., 72, 4 (1960); W. Baker and J. F. W. McOmie in "Non-Benzenoid Aromatic Compounds," D. Ginsburg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, p. 43.
(3) G. F. Emerson, L. Watts, and R. Pettit, J. Am. Chem. Soc., 87, 133 (1965).