The chemical properties described indicate structure II for the compound, differing from penicillin N only in configuration at C_6'. We propose the name isopenicillin N for this antibiotic. Penicillin N has been described as a product of fermentation by *Cephalosporium* species, at least one member of which also is capable of producing cephalosporin C (IV)[10] concurrently with penicillin N. Penicillin N has not been reported as a product of *Penicillium* fermentation. Although both the *Penicillium* and *Cephalosporium* species are capable of synthesizing the 6-APA fragment (as evidenced by penicillin N from *Cephalosporium*) an antibiotic common to both species has not been described. The discovery of isopenicillin N suggests possible convergence of biosynthetic pathways; however, one differentiating factor may be stereochemistry of the aminoadipyl side chain. Arnstein and Morris[3] have found α-aminoadipic acid in extracts of *Penicillium* mycelium, the amino acid apparently possessing the L configuration. They also have reported isolation of δ-(α-aminoadipyl)-cysteinylvaline but did not determine configuration of the aminoadipyl component. A biosynthetic scheme was proposed by them, based on isolation of the tripeptide and earlier work on biosynthesis of penicillin.[11] The presence of isopenicillin N in *Penicillium* fermentations is consonant with results reported in a later article by Wolff and Arnstein[12] and confirms their speculations concerning the presence of such a molecule.

(10) G. G. F. Newton and E. P. Abraham, *Biochem. J.*, **62**, 651 (1956).

(11) For leading references, see (3) and (12).

(12) E. C. Wolff and H. R. V. Arnstein, *Biochem. J.*, **76**, 375 (1960). KB 45

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1,8-BISDEHYDRO[14]ANNULENE, AN UNUSUAL AROMATIC COMPOUND[1]

Sir:

It has been reported that the oxidative coupling of *trans,trans*-4,10-tetradecadiene-1,7,13-triyne with cupric acetate in pyridine and subsequent treatment with potassium *t*-butoxide in *t*-butyl alcohol yielded two isomers of monodehydro[14] annulene (cyclotetradecahexaen-yne).[2] The isomer obtained in larger amount (which on partial hydrogenation had led to [14]annulene[2,3]) by nuclear magnetic resonance (n.m.r.) spectroscopy was subsequently shown to be a monodehydro[14] annulene containing 4 *cis* and 2 *trans* double bonds (*e.g.*, I).[4] It now has been found that the minor product is not an isomer of I, but in fact is 1,8-bisdehydro[14]annulene(II),[5] an unusual aromatic compound which can only be represented by cumulene containing Kekulé resonance forms.

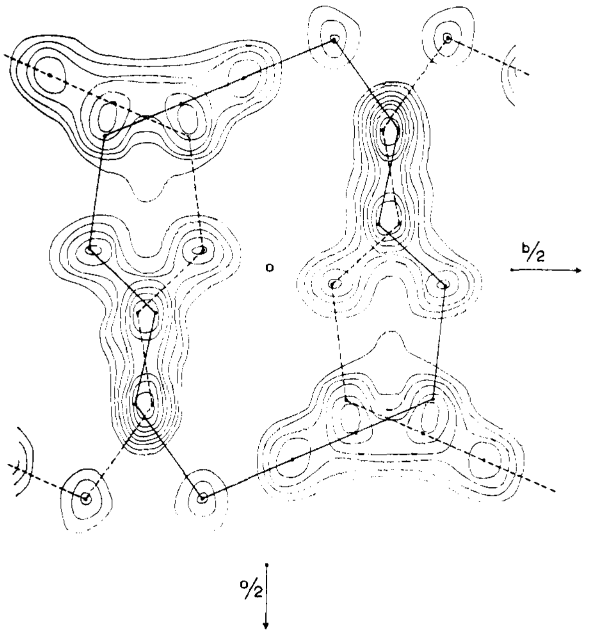
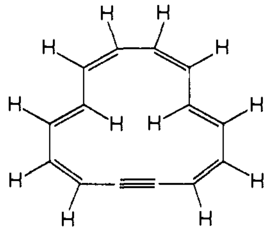
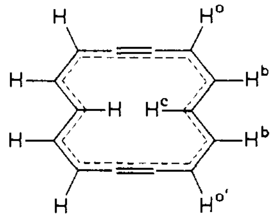


Fig. 1.—1,8-Bisdehydro[14]annulene (II): the electron density synthesis ρ(*XYO*). The broken lines refer to molecules related by symmetry to the reference molecule.



I



II

The n.m.r. spectrum of 1,8-bisdehydro[14]annulene (II) in deuteriochloroform solution (determined with a Varian V 4300 spectrometer operating at 60 Mc/sec.) consists of three multiplets at 15.54, 1.57 and 0.45τ, with relative intensities of 2:4:4. Thus, the substance possesses 10 rather than 12 protons. The presence of two groups of equivalent protons suggests that the molecule is symmetrical, and this is supported by the fine structure of the multiplets, which also shows two blocks of five contiguous C–H groups each to be present. The band at 15.54 τ is assigned to H^c (see formula II), since these protons should experience strong shielding by the secondary magnetic field arising from the ring current. This band is a symmetrical triplet, with $J = 13.3$ c./s. This coupling constant also appears in the band at 0.45 τ, which is a double doublet, and is assigned to H^b and $H^{b'}$. The second splitting ($J = 8.0$ c./s.) of the 0.45 τ band is equal to that observed for the band at 1.57 τ, which is a doublet and must arise from H^a and $H^{a'}$. The relative values of J_{ab} and of J_{bc} are indicative of *cis*- and *trans*-interactions, respectively,

(1) This is part XXIX in the Weizmann Institute series "Unsaturated Macrocyclic Compounds." For part XXVIII, see F. Sondheimer and D. A. Ben-Efraim, *J. Am. Chem. Soc.*, in press.

(2) F. Sondheimer and Y. Gaoni, *ibid.*, **82**, 5765 (1960).

(3) J. Bregman, *Nature*, **194**, 679 (1962).

(4) L. M. Jackman, F. Sondheimer, Y. Amiel, D. A. Ben-Efraim, Y. Gaoni, R. Wolovsky and A. A. Bothner-By, *J. Am. Chem. Soc.*, in press.

(5) Although the original elemental analysis of II[3] had supported a monodehydro[14]annulene structure, another analysis (found: C, 93.94; H, 6.02) was more in accord with a $C_{14}H_{10}$ formula (calcd.: C, 94.34; H, 5.66) than a $C_{14}H_{12}$ formula (calcd.: C, 93.29; H, 6.71).

although the absolute magnitudes of these coupling constants are substantially lower than usual. This analysis of the n.m.r. spectrum, together with the fact that full hydrogenation yielded cyclotetradecane,[2] uniquely defines the structure and stereochemistry of the substance as II.

An X-ray crystallographic analysis of 1,8-bisdehydro[14]annulene (II) shows the crystals (from chloroform) to be monoclinic, $a = 8.685 \pm 0.012$ Å., $b = 7.789 \pm 0.008$ Å., $c = 8.086 \pm 0.010$ Å., $\beta = 113° 48'$; the space group is $P2_1/c$ (C^5_{2h}), which, with two molecules of $C_{14}H_{10}$ per unit cell, corresponds to a density of ρ calcd. = 1.182 g./cc. The unit cell dimensions and space group require that the molecule is centrosymmetric in the crystal. The crystal structure has been determined by trial and error, Fourier and least square methods, and fully confirms structure II (see Fig. 1). Accurate bond lengths and bond angles cannot, as yet, be reported, since rotational disordering of the molecules in the lattice, as indicated by diffuse scattering and large calculated Debye factors, has not been explicitly considered in the refinement analysis. A three-dimensional analysis of the crystal structure at 90°K. is being undertaken to obtain more accurate bond distances, and will be reported later (by N.A.B. and R.M.). At this stage, it is already apparent that all the carbon atoms are coplanar (± 0.03 Å.).

The striking difference in the chemical shifts of the inner and outer protons in the n.m.r. spectrum, together with the over-all geometry of the molecule as determined by the X-ray crystallographic analysis, clearly establishes 1,8-bisdehydro[14]annulene to be aromatic. This is in keeping with expectation, since Hückel's rule is obeyed and the carbon skeleton is coplanar. The substance proved to be unusually stable; *e.g.*, it was completely unchanged after being kept for 1 month in the solid state at room temperature without protection from daylight. Also noteworthy is the position of the highest wave length maximum in the ultraviolet at 586 mμ (in isoöctane).[2]

Various aspects regarding the properties and synthesis of 1,8-bisdehydro[14]annulene are now under investigation. These include magnetic and theoretical studies of the electron distribution in the molecule, as well as the nature of the dehydrogenation involved in its formation.

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MEASUREMENT OF VERY FAST REACTION RATES BY RAMAN LINE BROADENING

Sir:

Line broadening measurements in magnetic resonance spectroscopy have been widely used to measure rates of fast chemical reactions.[1] It has been suggested[2] that line broadening techniques could also be used with various kinds of optical spectroscopy to measure the rates of even faster reactions. This has now been achieved, using Raman spectra. The range of usefulness seems to be for processes with half times from $\sim 10^{-11}$ to $\sim 10^{-14}$ sec. The latter probably is outside the range of chemical interest but the former is not, and for such rates the present method seems to be, by far, the most convenient when it is applicable. The present communication describes its application to the rate of proton transfer to trifluoroacetate ion from trifluoroacetic acid, probably *via* the hydronium ion, in aqueous solution.

Theory.—The Raman transition is assumed to involve degrees of freedom of the molecule which do not take part in the exchange. The effect of the exchange is to cause a time-dependence of the effective Hamiltonian "seen" by the portion of the molecule of interest: $H_{\text{eff}} = H_{\text{n}}$ when the molecule is in form n (n = 1, 2). A representation is used in which H_1 is diagonal, and off-diagonal elements of $(H_1 - H_2)$ are neglected.

The problem can now be treated by means of a simple generalization of the methods of Heitler.[3,4] In second-order time-dependent perturbation theory, the probability amplitude, b_{f}, for a transition in which the molecule changes its state and the angular frequency of a photon is decreased by ν obeys the equation

$$i\hbar\dot{b}_{\text{f}} = K_{\text{fo}}(t)\exp[i\int_0^t \omega_{\text{fo}}(t')\text{d}t'] - i\hbar\beta(t)b_{\text{f}} \quad (1)$$

Eq. (1) is to be compared with Heitler's eqs. (12) and (13).[3] The last term represents the broadening due to the natural line width. Otherwise, the only difference is in the time-dependence of K_{fo} and ω_{fo} due to the exchange. When the molecule is in form *n*, $K_{\text{fo}}(t) \equiv K_{\text{n}}$, $\omega_{\text{fo}}(t) \equiv \omega_{\text{n}} - \nu$, $\beta(\text{t}) \equiv \beta_{\text{n}}$. An explicit expression for K_{fo} is given by Heitler's eq. (7).[4]

The Raman intensity at frequency ν is given by eq. (2).

$$I(\nu)\text{d}\nu = 2Ad\nu \lim_{t \to \infty} \langle \beta(t) \ |b_{\text{f}}(t)|^2 \rangle \quad (2)$$

Here ⟨ ⟩ indicates an average and A is a constant.

In the present case, the molecule jumps randomly back and forth between forms 1 and 2. If τ_{n} is the mean time of a single sojourn in form n, $1/\tau_1$ is k_1, the (pseudo) first-order rate constant for the reaction (form 1) → (form 2).

Equations (1) and (2) have been solved for the case of relatively slow exchange: $|\omega_1 - \omega_2|\,\tau_{\text{n}} >> 1$, and all $\beta_{\text{m}}\tau_{\text{n}} >> 1$. Since $|\omega_1 - \omega_2|$ may be as large as several hundred cm.$^{-1}$, this approximation should hold fairly well until τ_1 and τ_2 approach 10^{-14} sec. The result is eq. (3). Simplification

$$I(\nu) = \frac{2A}{\hbar^2}\left\{\left(\frac{\tau_1}{\tau_1 + \tau_2}\right)|K_1|^2 \frac{\beta_1 + 1/\tau_1}{(\nu - \omega_1)^2 + (\beta_1 + 1/\tau_1)^2} + \left(\frac{\tau_2}{\tau_1 + \tau_2}\right)|K_2|^2 \frac{\beta_2 + 1/\tau_2}{(\nu - \omega_2)^2 + (\beta_2 + 1/\tau_2)^2}\right\} \quad (3)$$

results if $|K_2|^2 << |K_1|^2$, or if $|\omega_1 - \omega_2| >> \beta_{\text{n}} + 1/\tau_{\text{n}}$. In these cases it is shown readily that eq. (4) gives

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[1] H. Strehlow, in "Investigation of Rates and Reaction Mechanisms, Part II," S. L. Friess, E. S. Lewis and A. Weissberger, Editors, Interscience Publishers, Inc., New York, N. Y., 1962, Chapter 7.

[2] M. Eigen, private conversations.

[3] W. Heitler, "The Quantum Theory of Radiation," 3rd edition, Clarendon Press, Oxford, 1954, pp. 136–145.

[4] *Ibid.*, pp. 189–196.