For example, reduction of the octalone I[2] (R = CH_3, R′ = OCH_3, R″, R‴ = H) with lithium–ammonia in the presence of alcohol, then without separation of intermediates an oxidation and Wolff–Kishner reduction gave a 2-methoxy-10-methyldecalin in 65% over-all yield from the octalone. Vapor phase chromatography showed two components (A = 84 ± 3%; B = 16 ± 3%) which are *both trans*-decalins[3]: degradation of A and B separately by acetolysis with anhydrous hydrogen bromide in acetic acid, hydrolysis to the 10-methyl-2-decalol and oxidation with nitric acid readily gave *in both cases trans*-1-methylcyclohexane-1,2-diacetic acid, m.p. 197.4–198.8°,[4] undepressed on admixture with authentic material, but depressed to 164° when mixed with the pure *cis* isomer,[5] m.p. 191.2–192.9°.

Similarly, the octalone I[2] (R, R″ = CH_3, R′ = OCH_3, R‴ = H) gave by the same sequence of steps as outlined above substances of the *trans* decalin series: nitric acid oxidation of the final hydroxy compound gave again pure *trans*-1-methylcyclohexane-1,2-diacetic acid, m.p. and mixed m.p. 193.9–195.8°.

One last case may be mentioned from the literature[6]: Reduction of the optically active octalone I (R, R‴ = CH_3, R″ = *i*-Pr, R′ = H) with lithium and ammonia gave a decalone which was shown to be *trans* by rotatory dispersion.[7]

In the first of these three cases, the *cis* and *trans* decalones should be of roughly equal energy while in the last two cases the *cis* isomer should be the more stable one by between three and four kilocalories and thermodynamic stability of the products is clearly not controlling. The results are, however, in agreement with the formation of the more stable of the two isomers with the C_{10} hydrogen axial to the ketone ring.

(2) The synthesis of these substances is unexceptional and will be detailed in our full paper.

(3) These two substances differ in the relative stereochemistry of the methyl and methoxyl groups and reflect a similar mixture in their octalone precursor. The latter was made by methyl vinyl ketone addition to 2-methyl-4-methoxycyclohexanone and the major component is undoubtedly that resulting from (unhindered) axial addition of methyl vinyl ketone to the anion of the cyclohexanone. In this isomer the methyl and methoxyl groups are *cis*.

(4) Some confusion exists in the literature on the properties of this substance. Our authentic material was made by nitric acid oxidation of crystalline *trans*-5-methyl-2-decalol and gave correct analytical values.

(5) R. P. Linstead, A. F. Millidge and A. L. Walpole, *J. Chem. Soc.*, 1140 (1937).

(6) R. Howe and F. J. McQuillin, *ibid.*, 2670 (1956).

(7) Private communication from Professor Carl Djerassi.

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RECEIVED JANUARY 22, 1960

STEREOCHEMISTRY OF A BASE-CATALYZED EXCHANGE OF ETHYLBENZENE-α-*d*

Sir:

Cram, Kingsbury and Rickborn[1] recently have reported a high degree of retention of configuration in the replacement of a tertiary hydrogen by deuterium or *vice versa* in reaction with potassium *t*-butoxide in *t*-butyl alcohol. We report herewith that similar results are obtained for replacement of a secondary hydrogen by hydrogen in cyclohexylamine as solvent.

Optically active ethylbenzene-α-*d* both loses deuterium and racemizes with lithium cyclohexylamide in cyclohexylamine. Racemization can occur from replacement of deuterium by hydrogen (k_D) and in some fraction, λ, of the replacements of the α-hydrogen by hydrogen (k_H)

$$k_{rac} = k_D + \lambda k_H \qquad (1)$$

Determination of λ characterizes the stereochemistry of the reaction; λ = 0, 1 or 2 for complete retention, racemization or inversion, respectively.

At 49.9° with 0.049 *M* lithium cyclohexylamide and 0.71 *M* ethylbenzene-α-*d*, good pseudo-first order kinetics are obeyed using vacuum line techniques; k_{rac} and k_D are 3.0×10^{-5} and 1.07×10^{-5} sec.$^{-1}$, respectively. k_H cannot be measured directly but this rate constant can be determined from the primary isotope effect using tritium. Under similar conditions a mixture of ethylbenzene-α-*d* and ethylbenzene-α-*t* gave $k_D/k_T = 3.0 \pm 0.3$.[2] From the treatment of Swain, *et al.*,[3] we can derive

$$k_H/k_D = (k_D/k_T)^{2.26} \qquad (2)$$

whence $k_H/k_D = 12 \pm 3$.

All of the rate constants in equation 1 are now known. Evaluation of λ gives 0.17; *i.e.*, the replacement of the α-hydrogen by hydrogen under these conditions occurs with 17% racemization and 83% net retention of configuration. This relatively large degree of retention agrees with Cram's evaluation of amines as "retention solvents" in some other reactions thought to proceed through intermediates of the carbanion type.[4]

(2) This relatively large value has been confirmed recently with toluene-α-*d* and toluene-α-*t*, for which k_D/k_T = 2.75, 2.98 (W. C. Langworthy).

(3) C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr., and L. J. Schaad, THIS JOURNAL, **80**, 5888 (1958).

(4) D. J. Cram, A. Langemann, J. Allinger and K. P. Kopecky, *ibid.*, **81**, 5740 (1959).

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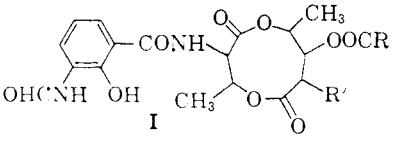
RECEIVED JANUARY 18, 1960

THE CHEMISTRY OF ANTIMYCIN A. IX. STRUCTURE OF THE ANTIMYCINS

Sir:

As the culmination of our extended structural studies on the members of the antimycin complex,[1]



I

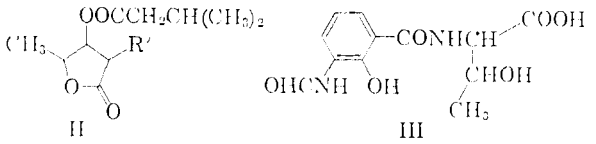
R = $CH_2CH(CH_3)_2$
(a) R′ = *n*-C_4H_9
(b) R′ = *n*-C_6H_{13}

we present findings which permit assignment of the generalized expression I to this group of closely related *Streptomyces* antibiotics.

(1) For paper VIII and preceding references, see W. Liu, E. E. van Tamelen and F. M. Strong, THIS JOURNAL, **82**, April 5 (1960).

(1) D. J. Cram, C. C. Kingsbury and B. Rickborn, THIS JOURNAL, **81**, 5835 (1959).

As previously shown,[2] mild aqueous alkaline treatment converts the non-basic antimycin to the antimycin lactone (II)[1,3] and—depending on conditions—either formic acid and antimycic acid,[1,4] or *ar*-N-formylantimycic acid (blastmycic acid) (III).[5] The infrared spectrum of antimycin A_1-



II III

($C_{28}H_{40}N_2O_9$) or antimycin A_3 (blastmycin) ($C_{26}H_{36}N_2O_9$)[6] in chloroform displays carbonyl absorption due to ester (5.73 μ), N-formyl (5.90 μ) and NH-acyl (6.09, 6.56 μ) functions, and reveals that a five-membered lactone ring is absent.[1-5] The ultraviolet spectra of antimycin A_1 (λ_{max} (alc.) 226, 320 mμ log ϵ 4.54, 3.68) and III (λ_{max} (alc.) 223, 318 mμ log ϵ 4.43, 3.76) are nearly identical, as are the spectra of antimycin A_3 (phenolic) methyl ether (Ic), m.p. 109–110° (C, 60.60; H, 7.03; OCH_3, 5.75) and the methyl ether methyl ester (non-crystalline) (IIIa) of III (both λ_{max} (alc.) 220, 294 mμ, shoulder at 215 mμ). Further, in the 5–7 μ region of the infrared, IIIa (5.74, 5.89, 6.01, 6.23 (w), 6.31 and 6.60 μ) and Ic (5.73, 5.88, 6.00, 6.23 (w), 6.31 and 6.60 μ) are virtually superimposable. These comparisons demonstrate the presence in the antibiotic of the *o*-OH-*m*-NHCHO-C_6H_3-CONH-system, isolated from other chromophores.

Conversion of antimycin A_1 by ammonia to N-formylantimycyl amide, m.p. 189.5–191° (C, 51.55; H, 5.43; N, 15.07) shows that the antimycic acid carboxyl group is masked in the intact antibiotic. Hot alcoholic hydrochloric acid serves only to transform the antibiotic to deformylantimycin A_1 hydrochloride, m.p. 190–191° dec. (C, 58.10; H, 7.36; infrared peaks at 5.72, 6.02 and 6.57 μ), which regenerates the parent material on treatment with formic acid. Such behavior renders unlikely structures which bind the potential carboxyl groups of II and III in the form of (a) hemi-ketal esters, or O-acyl derivatives of (b) ketone enols, (c) 1,3-dicarbonyl enols or (d) ester enols. Type (c) esters also are excluded by the ultraviolet data listed above; and the absence of an infrared peak below 5.73 μ[7] supports the conclusion that type (b) and (d) esters do not form part of the antimycin system.

Attempts to detect either a ketonic or an alcoholic function in antimycin have been, without exception, unavailing. For example, antimycin O-methyl ether is unchanged on attempted acetylation or chromic acid oxidation. Antimycin itself is not convertible to carbonyl derivatives; is not hydrogenated over platinum in acetic acid in the presence of hydrochloric acid; and is only deformylated on attempted mercaptanolysis. Further, the infrared spectrum of deformyl antimycin hydrochloride (in chloroform) shows the absence of a ketone carbonyl group. We conclude that the antimycin system is dilactonic, and represented by structure I. This expression replaces earlier proposals,[5,8] and taken together with previous findings[1-5] requires the specific structure Ib for antimycin A_1, and Ia for antimycin A_3.

(2) G. M. Tener, F. M. Bumpus, B. R. Dunshee and F. M. Strong, THIS JOURNAL, **75**, 1100 (1953).

(3) E. E. van Tamelen, F. M. Strong and U. C. Quarck, *ibid.*, **81**, 750 (1959).

(4) G. M. Tener, E. E. van Tamelen and F. M. Strong, *ibid.*, **75**, 3623 (1953).

(5) H. Yonehara and S. Takeuchi, *J. Antibictics (Japan)*, Ser. A, **11**, 122, 254 (1958).

(6) W. Liu and F. M. Strong, THIS JOURNAL, **81**, 4387 (1959).

(7) See H. H. Wasserman and P. S. Wharton, *Tetrahedron*, **3**, 321 (1958), and references cited therein.

(8) Strong, "Topics in Microbial Chemistry," Squibb Lectures on Chemistry of Microbial Products (1956), John Wiley and Sons, Inc., New York, N. Y., 1958, Vol. I, p. 1.

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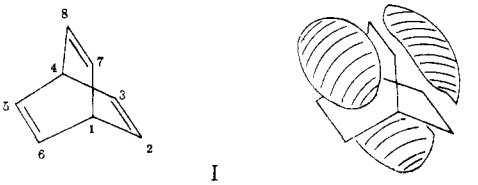
RECEIVED FEBRUARY 13, 1960

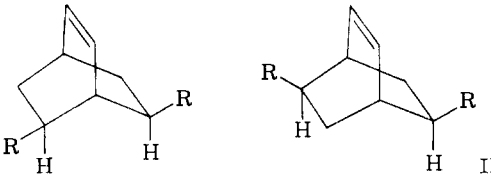
BICYCLO[2,2,2]-2,5,7-OCTATRIENE (BARRELENE), A UNIQUE CYCLIC SIX ELECTRON Pi SYSTEM

Sir:

Recently there has been considerable interest in bicyclo-[2,2,2]-2,5,7-octatriene (I) as a result of the possibility, first noted by Hine,[1] that this molecule might be aromatic. We now report the synthesis of this molecule using α-pyrone and methyl vinyl ketone as basic starting materials. We suggest the name barrelene because of the barrel shaped electron cloud.



I



II III

a, R = $COCH_3$
b, R = $C(NOH)CH_3$
c, R = $C(NOTs)CH_3$
d, R = $NHCOCH_3$
e, R = NH_2
f, R = $^+N(CH_3)_3\ I^-$

α-Pyrone-5-carboxylic acid[2] was decarboxylated in 50–90% yield over copper at 650°, thus affording the critical and previously difficultly available[3] starting material α-pyrone in large quantity.[4]

A decarboxylative double diene synthesis was effected by heating α-pyrone with excess methyl vinyl ketone, affording both 5,7-diacetylbicyclo-[2,2,2]-2-octene (IIa) and 5,8-diacetylbicyclo[2,-2,2]-2-octene (IIIa). The solid isomer, m.p. 85–86°, tentatively assigned the more symmetrical

(1) J. Hine, *et al.*, THIS JOURNAL, **77**, 594 (1955).

(2) *Org. Syn.*, **31**, 23 (1951).

(3) *E.g.*, v. Pechmann, *Ann.*, **264**, 272 (1891).

(4) The essentials of this procedure resulted from exploratory research of Mr. T. Beckmann with H. E. Z. We also are indebted to Mr. D. Paskovich for devoting two weeks of his research time to developing a scaled up procedure.