3 - acetoxy - 7α - fluoro - 1,3,5(10) - estratriene - 6,17-dione. The orientation and configuration of the substituents at C-6 and C-7 of X point to the intermediate B′ in the formation of X by bident α-attack of PF on IX.[7a,c]

(7) (a) Supported by American Cancer Society Grant P-265A; (b) Postdoctoral Fellow; (c) presented in part at the 2nd International Symposium on Fluorine Chemistry, Estes Park, Colorado, 1962.

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RECEIVED OCTOBER 16, 1962

SYNTHESIS OF CYCLOPROPENONES BY A MODIFIED FAVORSKII REACTION

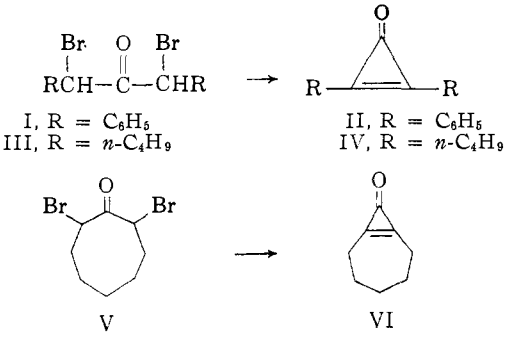
Sir:

The Favorskii reaction of α-haloketones with base has been shown to proceed through an intermediate with the symmetry of a cyclopropanone in at least some cases.[1,2,3] We wish to report[4] that under some conditions a cyclopropanone can be intercepted, when the starting material is a dibromo ketone, by dehydrobromination to the very stable cyclopropenone system. This is much more convenient than the types of syntheses reported previously[5,6,7] for cyclopropenones.

Treatment of α,α'-dibromodibenzyl ketone (I) (either the pure isomer, m.p. 112–114°,[8] or the mixture of *d,l*- and *meso*-compounds, m.p. 79–85°) with excess 20% triethylamine in methylene chloride at room temperature for 30 min. affords 50–60% yields of diphenylcyclopropenone (II),[5,6] best isolated by silica gel chromatography. The reaction also can be applied to the synthesis of cyclopropenones bearing only aliphatic substituents. Thus α,α'-dibromodi-*n*-amyl ketone (III) b.p. 101–106° (0.7 mm.), ($C_{11}H_{20}OBr_2$: C, 40.26; H, 6.14; Br, 48.72. Found: C, 40.46; H, 6.41; Br, 48.42; n.m.r. shows that this is a mixture of the *meso* and *d,l* compounds, with triplets at 5.45 and at 5.60 τ in addition to the other expected peaks), was treated with a 40:1 mixture of chloroform and triethylamine at reflux for 48 hr. A 12% yield of dibutylcyclopropenone (IV) was obtained, b.p. 95–97° (0.3 mm.) ($C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.72; H, 11.27). In the infrared the compound has the expected absorption at 1850 and 1660 cm.$^{-1}$; in the n.m.r. the methylenes attached to the cyclopropene ring are found as a triplet at 7.6 τ, with the remaining protons as a multiplet at 8.6 τ (methylenes) and a triplet at 9.15 τ (methyls).

The reaction can be extended to prepare other dialkylcyclopropenones. Interestingly, it also can be applied to dibromocycloöctanone. When 2,8-dibromocyclooctanone[9] (V) was heated under N_2 at 90° in a closed system with a 50% excess of 5% triethylamine in chloroform a 50% yield of cycloheptenocyclopropenone (VI) was obtained, m.p. 52–53° ($C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.85; H, 8.15). The material sublimes at 45° (1.5 mm.). In the infrared the compound shows the expected strong bands at 1840 and 1640 cm.$^{-1}$, and the n.m.r. spectrum confirms the structure. A four-proton triplet at 7.45 τ is assigned to the methylene groups attached to the ring, while a six-proton multiplet at 8.22 τ is found for the remaining protons. With refluxing aqueous KOH solution this compound affords cycloheptene-1-carboxylic acid, identical with an authentic sample.[9] It is hoped that VI may serve as a source of gas-phase cycloheptyne; in common with other cyclopropenones[5,6,7] VI loses carbon monoxide on pyrolysis, although in the case of VI rather high temperatures (250°) are required. Among other products, a 16% yield of tris-cycloheptenobenzene can be isolated from this pyrolysis, m.p. 184–185° ($C_{21}H_{30}$: C, 89.47; H, 10.48; mol. wt., 282. Found: C, 89.29: H, 10.71: mol. wt., 279, CCl_4 vapor pressure). In the ultraviolet the benzene has λ_{max} 274 mμ (ϵ = 262) while the n.m.r. spectrum shows the expected multiplets centered at 7.30 and 8.45 τ in a ratio of 2:3.

So far we have failed to prepare either unsubstituted cyclopropenone or cyclohexenocyclopropenone by application of our reaction conditions to appropriate haloketones. However, in both of these cases the difficulty might well lie with instability of the desired products rather than any failing of the synthetic method. Accordingly, our procedure promises to be of general use in the preparation of cyclopropenones.



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RECEIVED NOVEMBER 17, 1962

THE CHEMISTRY OF BLUENSOMYCIN. II. THE STRUCTURE OF BLUENSOMYCIN

Sir:

A previous communication[1] gave the structure of bluensidine, one of the two products obtained by methanolysis of the antibiotic bluensomycin. The identity of the second fragment is now described, and a structure for bluensomycin is proposed.

This second fragment (I) (colorless prisms from methanol–ether, m.p. 108–111°, $[\alpha]^{25}D$ −147° (*c*,1, water), $C_{14}H_{26}O_8N$,[2] one C-CH_3, one N-CH_3 (pK_a' 7.87) and one O-CH_3 group) appeared to be the methyl glycoside of an aminodisaccharide. Acetylation (pyridine–acetic anhydride) gave colorless prismatic needles (II), m.p. 195.5–197°, $[\alpha]^{25}D$ −124° (*c*, 1, $CHCl_3$). Analysis of this neutral product indicated $C_{12}H_{15}O_4(OCOCH_3)_4(N\langle^{CH_3}_{COCH_3}\rangle)(OCH_3)$. A close similarity was found to exist between the properties of II and those reported for methyl pentaacetyldihydrostreptobiosaminide, obtained by several laboratories from the methanolysis of dihydrostreptomycin.[3–6] Since

(1) Cf. A. Kende, *Organic Reactions*, **11**, 261 (1960).
(2) G. Stork and I. Borowitz, *J. Am. Chem. Soc.*, **82**, 4307 (1960); H. House and W. F. Gilmore, *ibid.*, **83**, 3972, 3980 (1961).
(3) A. W. Fort, *ibid.*, **84**, 2620, 2625 (1962).
(4) Reported in part at the 17th National Organic Symposium, Bloomington, 1961. Support of this work by the National Science Foundation, the Petroleum Research Foundation, and the Sloan Foundation is gratefully acknowledged.
(5) R. Breslow, R. Haynie and J. Mirra, *J. Am. Chem. Soc.*, **81**, 247 (1959).
(6) M. Volpin, Yu. Koreshkov and D. Kursanov, *Izvest. Akad. Nauk*, SSSR, 560 (1959).
(7) R. Breslow and R. Peterson, *J. Am. Chem. Soc.*, **82**, 4426 (1960).
(8) E. Bourcart, *Chem. Ber.*, **22**, 1368 (1889). In this paper it is reported that treatment of the ketone with ethanolic magnesia yields a compound with empirical formula $C_{13}H_{10}O$, but the product is not described further!
(9) G. Hesse and F. Urbanek, *Chem. Ber.*, **91**, 2733 (1958).

(1) B. Bannister and A. D. Argoudelis, *J. Am. Chem. Soc.*, **85**, 119 (1963)
(2) Analytical values for all the compounds described in this paper were consistent with the indicated formulas.

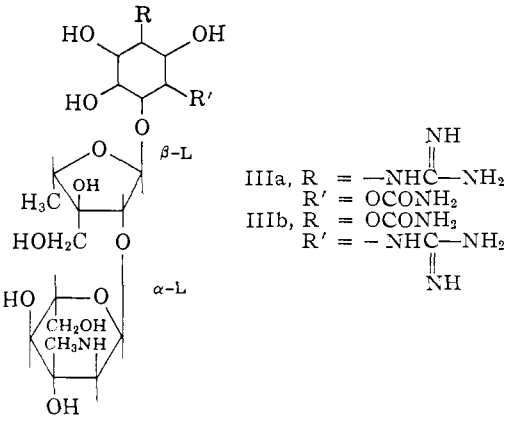
only the impure amorphous free methyl dihydrostreptobiosaminide has been described, no further comparison of data could be made.

An authentic sample of methyl dihydrostreptobiosaminide was now obtained crystalline from the methanolysis of dihydrostreptomycin trihydrochloride, and shown to be indistinguishable from I [m.p. and mixed m.p. 108–111°, $[\alpha]^{25}D$ −147° (*c*, 1, water)]. Acetylation gave α-methyl pentaacetyldihydrostreptobiosaminide,[5] identical with II [m.p. and mixed m.p., 197–198.5°, $[\alpha]^{25}D$ −120° (*c*, 1, chloroform)].

Degradation of I with concentrated hydrochloric acid gave an aminosugar which afforded (acetic anhydride–pyridine) a crystalline pentaacetate, m.p. 161–162°, $[\alpha]^{25}D$ −101° (*c*, 1, chloroform), identical with an authentic sample of pentaacetyl N-methyl-α-L-glucosamine.[6a]

Final confirmation of the structure of I was obtained by the mercaptolysis of bluensomycin dihydrochloride in ethyl mercaptan. Separation of bluensidine carbonate from the ethyl thioglycoside was achieved by carbon chromatography, and the amorphous product gave a crystalline pentaacetate, m.p. 115.5–116.5°, $[\alpha]^{25}D$ −170°, (*c*, 1, chloroform). Authentic ethyl pentacetylthiodihydrostreptobiosaminide[7] was obtained by the corresponding mercaptolysis of methyl dihydrostreptobiosaminide and acetylation, and the two samples proved to be identical in all respects.

Data presented in this and the previous communication point to a structure for bluensomycin in which bluensidine is linked glycosidically to dihydrostreptobiosamine by condensation of one of the four hydroxyl groups present in bluensidine with the hemi-acetal hydroxyl group present in dihydrostreptobiosamine. Comparative periodate oxidation of bluensomycin and dihydrostreptomycin hydrochlorides, which are identical in the disaccharide portion of their respective molecules, showed that both antibiotics consumed the same amount of periodate with identical rates and with production of the same amount of acid. This indicates that one glycol grouping is present in the bluensidine part of bluensomycin as it is in the streptidine part of dihydrostreptomycin. When dihydrostreptomycin and bluensomycin hydrochlorides were hydrolyzed with *N* aqueous hydrochloric acid at room temperature, the specific rotations of the solutions decreased from initial values of −93 and −92° to constant values of −73 and −71°, respectively, obtained after 52 hr. Under the conditions of hydrolysis, these antibiotics are cleaved to dihydrostreptobiosamine and to streptidine (optically inactive) and bluensidine ($[\alpha]^{25}D$ + 0.5 to 1.5°), respectively. This indicates that the glycosidic bond between bluensidine and dihydrostreptobiosamine in bluensomycin has the same configuration[8] as that between streptidine and dihydrostreptobiosamine in dihydrostreptomycin, limiting the possible structures for bluensomycin to IIIa and IIIb. It is of considerable interest that bluensomycin is the first member of the streptomycin family in which it has been found that the streptidine moiety has been replaced by



a different, though biogenetically-related, guanidine-containing base.

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ABNORMAL DIRECTION OF RING-OPENING OF A 2,3-ANHYDROFURANOSIDE[1a]

Sir:

The 2,3-anhydrofuranose sugars are some of the most useful intermediates for the preparation of unusual nucleosides and sugars. As examples the synthesis of 2′-deoxyadenosine,[2] of 9-(β-D-arabinofuranosyl)-adenine,[3] and of puromycin[4] all utilized a 2,3-anhydrofuranoside derivative as a key intermediate. In all cases studied to date, the opening of such a sugar or nucleoside epoxide by a nucleophile has occurred very predominantly at C.3[5] so that this has been accepted as the essentially invariable result of 2,3-anhydrofuranoside-opening: a rationalization of this reaction course has been presented.[6] This manuscript reports the first exception to this rule of very predominant C.3 opening of a 2,3-anhydrofuranoside.

The reaction of sodium benzyl mercaptide with methyl 2,3-anhydro-β-D-lyxofuranoside (III)[7] gave an essentially quantitative yield of a sirup that was treated with *p*-nitrobenzoyl chloride in pyridine. Fractional crystallization of the acylated mixture afforded two crystalline esters,[8] m.p. 91–92°, $[\alpha]^{25}D$ −114° (2% in chloroform) and m.p. 139–140°, $[\alpha]^{25}D$ +11° (2% in chloroform). The assignment of structures I and IV, respectively, to these two compounds was based on the comparison of their n.m.r. spectra with those of the corresponding diols (II and V) obtained by saponification, and of the corresponding diacetates.

(1) (a) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service, Contract No. SA-43-ph-1892. The opinions expressed in this paper are those of the authors and are not necessarily those of the Cancer Chemotherapy National Service Center. (b) Istituto di Chimica Farmaceutica e Tossicologica, Università di Roma (Italy); holder of a NATO fellowship during 1962.

(2) C. D. Anderson, L. Goodman and B. R. Baker, *J. Am. Chem. Soc.*, **81**, 3967 (1959).

(3) W. W. Lee, A. Benitez, L. Goodman and B. R. Baker, *ibid.*, **82**, 2648 (1960).

(4) B. R. Baker, R. E. Schaub, J. J. Joseph and J. H. Williams, *ibid.*, **76**, 4044 (1954).

(5) See C. D. Anderson, L. Goodman and B. R. Baker, *ibid.*, **81**, 898 (1959), for a discussion of this point.

(6) R. E. Schaub and M. J. Weiss, *ibid.*, **80**, 4683 (1958).

(7) B. R. Baker, R. E. Schaub and J. H. Williams, *ibid.*, **77**, 7 (1955).

(8) Satisfactory analytical data were obtained for all the compounds reported herein.

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(6a) Prepared from N-methyl-L-glucosamine, kindly provided by Dr. H. E. Renis of The Upjohn Company.

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(8) M. L. Wolfrom, M. J. Cron, C. W. DeWalt and R. M. Husband, *ibid.*, **76**, 3675 (1954).