non-phosphorylative, may well effect the transfer of fructose into the cell.

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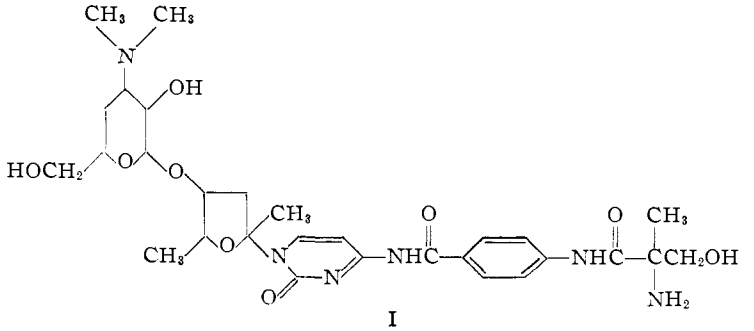
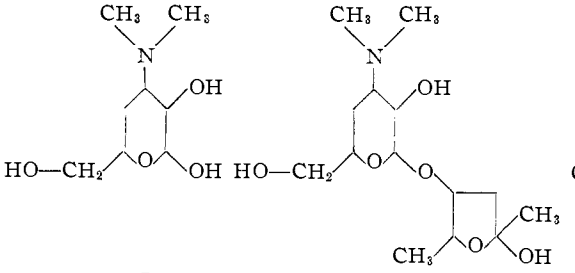
THE STRUCTURE OF AMICETIN. A NEW DIMETHYLAMINO SUGAR

Sir:

Structure I, which incorporates the new dimethylamino sugar *amosamine* (II), is presented for the antibiotic amicetin. In 1953, Flynn, Hinman, Caron and Woolf[1] published evidence in support of a partial structure for amicetin which included the α-methylserine, *p*-aminobenzoic acid, and cytosine moieties of structure I with an unknown C_{14} fragment attached to the 1-position of cytosine.

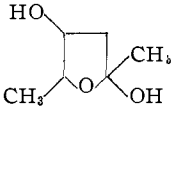


I



II

III



IV

From the acid hydrolysis of amicetin the C_{14} fragment was isolated as the crystalline hydrochloride, m.p. 170.5–171.5° (Calcd. for $C_{14}H_{27}NO_6 \cdot HCl$: C, 49.19; H. 8.26; N, 4.10; Cl, 10.37. Found: C, 49.14; H, 8.40; N, 4.12; Cl, 10.45), for which the name *amicetamine* and structure III[2] are proposed. Analysis of the amorphous free base indicated the presence of two N-methyl and two C-methyl but no O-methyl groups. The glycoside did not reduce Fehling or Benedict solution but possessed a potential carbonyl group as indicated by hydroxylamine titration although the infrared spectrum of the hydrochloride, when determined as a Nujol mull, did not show carbonyl absorption. The fact that the glycoside gave a positive iodoform test while cytosamine (the C_{14}-cytosine[1] moiety) did not indicated that the cytosine moiety was attached to C_{14} moiety III *via* a potential methyl ketone.

(1) E. H. Flynn, J. W. Hinman, E. L. Caron and D. O. Woolf, Jr., THIS JOURNAL, **75**, 5867 (1953).

(2) Reference 1 incorrectly reported the empirical formula of amicetin as $C_{29}H_{44}N_6O_9$ rather than $C_{29}H_{42}N_6O_9$ and consequently of the C_{14} portion as $C_{14}H_{28}NO_5$ rather than $C_{14}H_{26}NO_5$.

Aqueous sodium metaperiodate oxidized the glycoside III with the consumption of 2.7 to 2.9 moles in 24 hours. From these oxidations, dimethylamine was isolated as the *p*-hydroxyazobenzene *p'*-sulfonic acid salt, formic acid as the barium salt, glyoxal as the phenylosazone, formaldehyde as the dimedone derivative, and a small amount of acetaldehyde as the 2,4-dinitrophenylhydrazone derivative.

Glycoside III was hydrolyzed with the aid of a sulfonic acid resin (Dowex-50), and from the hydrolysis the dimethylamino sugar, amosamine (II), was isolated as the crystalline hydrochloride, m.p. 192–193° (calcd. for $C_8H_{17}NO_4 \cdot HCl$: C, 42.30; H, 7.97; N, 6.15; Cl, 15.57; mol. wt., 227.7. Found: C, 42.09; H, 8.13; N, 6.13; Cl, 15.18; mol. wt., 222), $[\alpha]^{25}D$ + 45.5 (1% in water). II reduced Fehling solution and consumed three moles of periodate from which one equivalent of formaldehyde could be isolated as the dimedone derivative and two equivalents of the volatile organic acid (formic) shown by titration. These data allow only a 2- or 4-deoxyaldohexose; the isolation of glyoxal from the C_{14} oxidation provides evidence for the 4-deoxy structure II. The dimethylamino group was shown to be in the 3-position (β-dimethylaminoaldehyde) by application of the procedure of Hochstein and Regna,[3] which compares the instability of various amino sugars in alkali; under the conditions they describe II lost 43% of one equivalent of dimethylamine in two hours.

The structure of the neutral moiety IV was deduced from the following data. The stable hemiketal structure for III demands a pyranose or furanose ring; the fact that the two C-methyl groups must reside in IV indicates the furanose form of IV in the glycoside III as well as in the antibiotic I. The position of the remaining methyl and hydroxyl groups in IV was determined by periodate oxidations. Cleavage of amicetin with methanolic hydrogen chloride followed by methanolysis (Dowex-50) of the resulting crude methyl glycoside of III gave a neutral fragment (IV methyl glycoside) which did not reduce periodate. The corresponding ketose IV consumed one equivalent of periodate from which 52% of acetaldehyde 2,4-dinitrophenylhydrazone could be isolated. These data allow only structure IV for the neutral moiety.

The cytosine was shown to be attached through the ketal carbon of IV by the iodoform tests. The reducing aminosugar must be attached, therefore, to the only remaining hydroxyl in IV *via* the aldehyde carbon to form the non-reducing glycoside III and the antibiotic amicetin I.

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(3) F. A. Hochstein and P. P. Regna, THIS JOURNAL, **77**, 3354 (1955).