his modification should not be considered a really fundamental improvement over the BET theory.

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## STREPTOMYCES ANTIBIOTICS. V. N-METHYL-*l*-GLUCOSAMINE FROM STREPTOMYCIN

*Sir:*

Streptomycin has been degraded to a new product which has been established as N-methyl-*l*-glucosamine.

Acid hydrolysis of methyl streptobiosaminide dimethyl acetal[1] followed by acetylation yielded a pentaacetyl derivative of a hexosamine; m. p. 160.5–161.5° (micro-block), $[\alpha]^{25}D$ −100° (*c*, 0.7 in chloroform). *Anal.* Calcd. for $C_{17}H_{25}NO_{10}$: C, 50.62; H, 6.25; N, 3.47; $CH_3CO$, 53.3; mol. wt., 403. Found: C, 50.51; H, 6.24; N, 3.76; $CH_3CO$, 49.2; mol. wt., 414 (cryoscopic in benzene). The hydrochloride of the hexosamine was obtained from the pentaacetyl derivative by hydrolysis with hydrochloric acid; m. p. 160–163° (micro-block), $[\alpha]^{25}D$ −103° (initial), −88° (final) (*c*, 0.6 in water). *Anal.* Calcd. for $C_7H_{15}NO_5 \cdot HCl$: C, 36.60; H, 7.02; $CH_3N$, 6.5. Found: C, 36.65; H, 6.86; $CH_3N$, 6.8. Treatment of the hydrochloride with silver oxide gave the free base as a colorless gum; $[\alpha]^{25}D$ −65° (*c*, 1.0 in methanol). Acetylation of the free base in the presence of methanol gave the N-acetyl derivative; m. p. 165–166° (micro-block), $[\alpha]^{25}D$ −51° (*c*, 0.4 in water).

The phenylosazone prepared from the hexosamine melted at 205° (capill.).[2] A phenylosotriazole, prepared[3] from this osazone, melted at the same temperature (196–197°) as the corresponding derivative of *d*-glucose, and the specific rotation was of equal magnitude but opposite in sign.

Oxidation of the free hexosamine with mercuric oxide gave an acid which had the same melting point (m. p. 230–232°) reported for N-methyl-*d*-glucosamic acid.[4] Again, the rotation was of the same magnitude but opposite sign.

Hydrolysis of the product of the reaction between *l*-arabinose, methylamine and hydrogen cyanide gave an acid which was identical with the "natural" acid described above. When the synthetic acid was converted to the lactone, reduced and acetylated, the product was found to be identical with the pentaacetyl derivative of the "natural" hexosamine. Thus, the configurations about $C_3$, $C_4$, and $C_5$ of the hexosamine are those at carbons 2, 3, and 4 of *l*-arabinose (or carbons 3, 4 and 5 of *l*-glucose).

Methylation of *d*-glucosamine, followed by acetylation, yielded pentaacetyl-N-methyl-*d*-glucosamine; m. p. 160.5–161.5° (micro-block), $[\alpha]^{25}D$ +101°. The properties of this compound are identical with those of the pentaacetyl derivative described above except for the sign of rotation.

With these data and the reported configuration of carbon atom 2 of *d*-glucosamine,[5] it is concluded that the configuration at carbon atom 2 of the hexosamine is also that of *l*-glucose and the degradation product is N-methyl-*l*-glucosamine.

(1) Brink, Kuehl and Folkers, *Science*, **102**, 506 (1945).

(2) *l*-Glucose phenylosazone, m. p. 205°; Fischer, *Ber.*, **23**, 374 (1890).

(3) Haskins, Hann and Hudson, THIS JOURNAL, **67**, 939 (1945).

(4) Votoček and Lukeš, *Chem. Listy*, **29**, 308 (1935).

(5) Haworth, Lake and Peat, *J. Chem. Soc.*, 271 (1939).

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## NEIGHBORING GROUPS AND REACTIVITY

*Sir:*

Heretofore, we have stressed the stereochemical consequences of participation by neighboring groups[1] such as OAc, Br, $OCH_3$, etc., in replacement reactions. We have recently completed rate measurements which bring out the striking connection between reactivity and this participation.

First order rate-constants of solvolysis at 75° in glacial acetic acid of a series of 2-substituted cyclohexyl *p*-bromobenzenesulfonates give the following relative reactivities: unsubstituted, 1.00; *trans*-2-OAc, 0.240; *trans*-2-Br, 0.101; *trans*-2-$OCH_3$, 0.057; *trans*-2-Cl, $4.9 \times 10^{-4}$; *cis*-2-OAc, $3.8 \times 10^{-4}$; *cis*-2-$OSO_2C_6H_4Br$, $7.7 \times 10^{-5}$; *trans*-2-$OSO_2C_6H_4Br$, $6.9 \times 10^{-5}$. Similarly, acetolysis rates at 23.6° of cyclohexyl *p*-toluenesulfonates give the relative reactivities: *trans*-2-I, 1800; unsubstituted 1.00.

The effects of a halogen substituent similar to those above are seen also in the rough values of relative reactivities of alcohols to fuming hydrobromic acid or concentrated hydrochloric acid at room temperature. One reactivity sequence obtained in this way is: *trans*-2-iodocyclohexanol 1000; cyclohexanol 1; *trans*-2-bromocyclohexanol 0.08; *trans*-2-chlorocyclohexanol $1.6 \times 10^{-4}$.

In the relatively reactive substituted cyclohexyl compounds (which are typical of most of the cases where stereochemical evidence for participation exists) the neighboring group supplies a large driving force for the rate-determining ionization of the departing group. This partially neutralizes or completely overbalances (as for I) the rate-retarding inductive effect. The sequence I > Br > Cl is to be expected. As in the case of the acetoxy group, the driving force is supplied from the *trans*-position and poorly if at all from the *cis*-position. In the case of the

(1) Winstein and Seymour, THIS JOURNAL, **68**, 119 (1946), and previous articles in the series.