mine water oxidation and hydrolysis, gave D-isoserine[8] (positive rotation,[7] isolated and identified from papergram) from C-4, C-5 and C-6 of neosamine C. These data assign neosamine C the same stereochemistry as that of D-glucosamine at C-2 and C-5.

It has been shown for a number of hexoses that the replacement of a hydroxyl group by an amino group does not alter appreciably the magnitude of their specific rotations.[8,9] The rotation of neosamine C dihydrochloride, $[\alpha]^{23}D$ +67°, thus suggests that it probably has the stereochemistry of D-glucose (D-glucosamine hydrochloride, $[\alpha]^{20}D$ +73°)[10] or, somewhat less likely, that of D-galactose (D-galactosamine hydrochloride, $[\alpha]^{20}D$ +96°),[10] but not that of D-gulose (D-gulosamine hydrochloride, $[\alpha]^{21}D$ −19°)[9] or D-allose ($[\alpha]^{20}D$ +14°),[11] the two other aldohexoses allowed by the stereochemical assignments at C-2 and C-5.

The high positive rotation of neobiosamine C (dihydrochloride: [M]D +33,700)[1] suggests[12,13] an α-D-glycosidic link between neosamine C (dihydrochloride: [M]D +16,800) and D-ribose ([M]D −3,450),[2] an assignment strengthened by an infrared band at 844 cm.$^{-1}$ in the spectrum of N,N'-dibenzoylneobiosaminol C, attributed[14] to equatorial (β) anomeric C—H deformation. The most probable stereochemistry of neobiosamine C is then represented by I.[3a]

Acid hydrolysis of methyl neobiosaminide B[1] gave hygroscopic neosamine B dihydrochloride, $[\alpha]^{27}D$ +17° (*c* 0.92, water)[15] [*Anal.* Found: C, 28.41; H, 6.61; N, 10.76], which gave positive reactions with ninhydrin, aniline acid phthalate and Fehling solution.

The isomeric neosamines B and C represent to our knowledge the first two diaminohexoses isolated, though mono-aminohexoses have been the subject of extensive recent investigations[8,17,18] and the related antibiotic kanamycin has been shown to contain both 6-amino-6-deoxy-D-glucose and 3-amino-3-deoxy-D-glucose.[18] Since other portions (neamine, D-ribose) of the isomeric neomycins B and C are identical, their isolation and non-identity allow the assignment of chemical[16] and antibacterial[16,19] differences of the two antibiotics to the neosamines.

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INTRAMOLECULAR ELECTRON EXCHANGE IN ANIONS OF PARACYCLOPHANES[1]

Sir:

As Cram and his co-workers have demonstrated,[2] the paracyclophanes are well suited for studies of inter-ring interactions. I have examined the anions of the [1.8], [2.2], [3.4], [4.4] and [6.6] paracyclophanes for inter-ring electron exchange by the method of electron magnetic resonance. The hyperfine structure in the magnetic resonance absorption of a paracyclophane anion appears to result from coupling with the nuclei in one ring only when the exchange is slow, and with the nuclei in both rings when the exchange is rapid. "Slow" and "rapid" are taken relative to the frequency of the hyperfine interaction. In the intermediate range the nature of the spectrum depends on the kinetics of the exchange.

The paracyclophane anions were prepared by reduction of solutions in 1,2-dimethoxyethane with alkali metals. The [1.8] and [2.2] compounds are reduced in good yield at room temperature by potassium. The [3.4] and [4.4] and [6.6] compounds on the other hand are appreciably (but incompletely) reduced only at temperatures below −50°. At room temperature only a blue diamagnetic solution of rubidium in the solvent is found. As the solution is cooled the blue color is replaced by the green color of the anions. The reaction is reversible, the blue color returning when the solution is warmed. The cycle may be repeated many times.

The magnetic resonance spectra of the anions indicate that the unpaired electron is found almost exclusively at the unsubstituted ring positions in accord with earlier observations of the anions of toluene and *p*-xylene.[3] $[1.8]^-$ has a spectrum of

(1) This work has been supported by the U. S. Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command under Contract AF 49-638-464. Reproduction in whole or in part is permitted for any purpose of the U. S. Government.

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nine evenly spaced lines with approximately binomial intensity distribution. The interval between lines is 2.7 oersteds. $[2.2]^-$ has a poorly resolved spectrum of at least nine components. $[4.4]^-$ and $[6.6]^-$ have indistinguishable spectra of five evenly spaced lines with binomial intensity distribution. The lines are completely resolved and are separated by 5.5 oersteds. $[3.4]^-$ has a spectrum resembling those of $[4.4]^-$ and $[6.6]^-$ but with wider lines and broad tails extending beyond the 22 oersted spread of the former. The spectra may be interpreted as follows: In $[4.4]^-$ and $[6.6]^-$ the electron exchange proceeds less frequently than 3×10^6 sec.$^{-1}$ (the line breadth in frequency), while in $[1.8]^-$ and $[2.2]^-$ it proceeds more rapidly than 1.5×10^7 sec.$^{-1}$ In [3.4] the exchange rate is somewhat higher than 3×10^6 sec.$^{-1}$ but less than 1.5×10^7 sec.$^{-1}$.

Further work on other paracyclophanes and on the temperature dependence of the rates is in progress.

I am deeply indebted to Professor Cram for all the paracyclophanes which have been used in these experiments.

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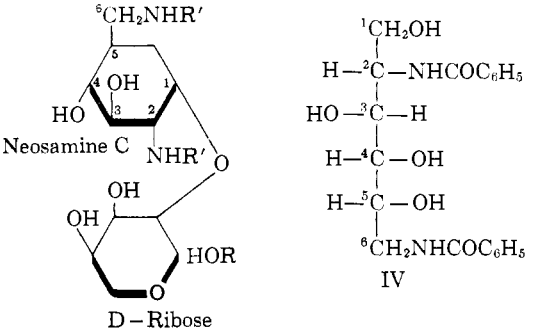
RECEIVED OCTOBER 4, 1958

CHEMISTRY OF THE NEOMYCINS. III. THE STRUCTURE OF NEOBIOSAMINE C

Sir:

It was reported recently[1,2] that neobiosamine C, approximately one-half of neomycin C, is a disaccharide composed of a diaminohexose (for which we now propose the name neosamine C, *cf.* accompanying Communication)[3] and D-ribose. We present here evidence showing neobiosamine C to have the structure I.



IV

I, R = R′ = H (Neobiosamine C)
II, R = CH_3, R′ = COC_6H_5
III, R = CH_3, R′ = H

Cleavage of the glycosidic linkage in methyl N,N′-dibenzoylneobiosaminide C[1] (II) by mild acidic hydrolysis,[2] followed by sodium borohydride reduction, gave N,N′-dibenzoylneosaminol C (IV), m.p. 186–188.5°. [Found: C, 61.80; H, 6.23; N, 7.28], which reduced two moles of sodium periodate with formation of no formaldehyde. The periodate product was oxidized with bromine water, then hydrolyzed vigorously, to give glycine [papergram—violet ninhydrin spot, R_f 0.445 (PyW),[4] 0.375 (PhenW)[4]; authentic sample—violet, R_f 0.446 (PyW), 0.363 (PhenW)] and serine [purple spot, R_f 0.531 (PyW), 0.305 (PhenW); authentic sample—purple, R_f 0.528 (PyW), 0.286 (PhenW)]. Methyl N,N′-dibenzoylneobiosaminide C(II) consumes two moles of periodate, thus must have one —CHOHCHOH— grouping in each monosaccharide (ribose and neosamine) moiety. This periodate oxidation product was treated with bromine water, then hydrolyzed vigorously to give isoserine [papergram—yellow ninhydrin spot, R_f 0.43 (PyW), 0.27 (PhenW); authentic sample—yellow, R_f 0.42 (PyW), 0.26 (PhenW)], as well as glycine [violet spot, R_f 0.39 (PyW), 0.34 (PhenW); authentic sample—violet, R_f 0.39 (PyW) 0.33 (PhenW)]. The formation of isoserine establishes an aldohexose (rather than a ketohexose) structure for neosamine C, while demonstration of a vicinal glycol grouping in this moiety of II shows neosamine C to contain a pyranose (rather than furanose) ring in I. The structure of neosamine C in neomycin C is, therefore, that shown in I.

Methyl neobiosaminide C[1] (III) was hydrolyzed under mild conditions to I, which was reduced with sodium borohydride, then N-benzoylated to give N,N′-dibenzoylneobiosaminol C, m.p. 217–227° dec. [Found: C, 56.12; H, 6.31; N, 5.10]. Vigorous hydrolysis of this derivative gave ribitol [papergram—colorless with aniline acid phthalate,[5] R_f 0.616 (BAW 221)[4]; authentic sample—colorless, R_f 0.612 (BAW 221)], thus confirming the earlier assignment[1] of neobiosamine C as a neosaminidoribose, rather than a ribosidoneosamine, which would have given ribose [authentic sample—red spot, R_f 0.584 (BAW 221)]. N,N′-Dibenzoylneobiosaminol C consumed three moles of sodium periodate, with formation of one mole of acid. A glycosidic bond to the ribose C-5 position would require a four-mole periodate uptake, with formation of two moles of acid. The ribose C-3 position is eliminated *per se* by the uptake of one mole of periodate in the ribose moiety of methyl N,N′-dibenzoylneobiosaminide C (*cf.* above), (impossible with a C-3 link since two adjacent hydroxyl groups are prohibited for either pyranose or furanose forms). The ribose C-4 position is also extremely unlikely, since oxidation of neobiosamine with bromine water gave a product whose infrared spectrum contains a carbonyl band at 1765 cm.$^{-1}$, indicative of a γ-lactone,[6] hence of a free C-4 hydroxyl. The sole remaining ribose position is C-2 and the structure of neobiosamine C is I.

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