ence of a chlorination inhibitor[5] to direct the fermentation from the production of 7-chlorotetracycline to the production of tetracycline. Again, the reduction product from added I was observed to be the chlorinated product, 7-chlorotetracycline.

Complete reduction of I never was observed despite the fact that, during the reduction periods, the organisms synthesized endogenous tetracyclines to the extent of 5 to 30 times the quantity of I reduced. This was not due to the presence of a large pool of I, since no appreciable quantities of I have been observed during fermentations of BC-41 and V-138. These organisms reduced I only when it was present during that phase of the fermentation in which endogenous tetracyclines were being actively produced. The biological reduction yielded only 7-chlorotetracycline; in contrast, catalytic hydrogenation, under previously reported conditions,[1] yielded both of the epimers at C.5a and removed chlorine.

It is suggested that 7-chloro-5a-(11a)-dehydrotetracycline is a precursor of 7-chlorotetracycline and that, possibly, the last step in 7-chlorotetracycline biosynthesis is the reduction of the 5a(11a) double bond in 7-chloro-5a(11a)-dehydrotetracycline.

(5) Y. Sekizawa, *The Journal of Biochemistry (Japan)*, **42**, No. 2, 217 (1955).

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RECEIVED NOVEMBER 6, 1958

A NEW EPOXY ALDEHYDE: SYNTHESIS OF GLYCIDALDEHYDE FROM ACROLEIN AND HYDROGEN PEROXIDE

Sir:

Although the epoxidation of α,β-unsaturated ketones by alkaline hydrogen peroxide is a well known procedure,[1] the corresponding reaction with *simple* α,β-unsaturated aldehydes has not been described.[2]

We wish to report the synthesis of glycidaldehyde (I) from acrolein and hydrogen peroxide. Equimolar amounts of these materials were combined at room temperature and added dropwise with stirring over 1 hour at 25–30° to an aqueous solution held at *p*H 8–8.5 by the continuous addition of *N* sodium hydroxide. After an additional 0.5 hour, titration for oxirane oxygen indicated an 82% yield of I. Anhydrous glycidaldehyde, a

$$H_2C{=}CH{-}CHO + H_2O_2 \longrightarrow \underset{\text{I}}{H_2C\overset{O}{\diagup\diagdown}CH{-}CHO}$$

compound heretofore not described in the chemical literature, was secured in 33% recovery by saturation of the reaction mixture with ammonium sulfate, extraction with warm cyclohexanone, and fractional distillation. It is a colorless stable liquid with a pungent odor having b.p. 112–113° (760 mm.) and 57–58° (100 mm.), $n^{20}D$ 1.4185, sp. gr.$^{20}_4$ 1.126. (Calcd. for $C_3H_4O_2$: C, 50.0; H, 5.6; oxirane oxygen, 22.2; carbonyl value, 1.39 equiv./100 g. Found: C, 50.1; H, 5.7; oxirane oxygen, 21.8; carbonyl value, 1.39 equiv./100 g.). The 2,4-dinitrophenylhydrazone derivative had m.p. 96–98° followed by resolidification and m.p. unsharp *ca.* 150° (Calcd. for $C_9H_8N_4O_5$: C, 42.9; H, 3.2; N, 22.2. Found: C, 42.9; H, 3.2; N, 22.1).

A 10% aqueous solution of glycidaldehyde underwent hydrolysis at a rate of about 0.4% per day when stored at 5°. The hydrolysis product, glyceraldehyde, had m.p. and mixed m.p. 136–138°.

Range finding acute toxicity studies place glycidaldehyde in a moderately toxic class by oral, vapor, and percutaneous routes.

Detailed investigations of both the synthesis and chemical reactions of glycidaldehyde have been carried out and will be reported at a later date.

(1) E. Weitz and A. Scheffer, *Ber.*, **54**, 2327 (1921); they obtained only acidic products from crotonaldehyde and cinnamaldehyde.

(2) 2,3-Diphenylacrolein has recently been epoxidized; see Absts. of the 134th A.C.S. Meeting, Sept. 7–12, 1958, p. 28-P.

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RECEIVED SEPTEMBER 2, 1958

CHEMISTRY OF THE NEOMYCINS. IV. ISOLATION OF NEOSAMINES B AND C. STEREOCHEMISTRY OF NEOBIOSAMINE C

Sir:

It has been shown that neobiosamine C,[1] from the antibiotic neomycin C, is a disaccharide composed of D-ribose[2] and a 2,6-diaminoaldohexose (neosamine C).[3] Neosamine C and the corresponding neosamine B (from neomycin B *via* neobiosamine B)[1] have now been isolated, and the most probable stereochemistry of neobiosamine C has been shown to be that represented by formula I.[3a]

Hydrolysis of methyl neobiosaminide C[1] (III)[3a] for 90 min. in refluxing 6*N* hydrochloric acid gave neosamine C dihydrochloride, $[\alpha]^{23}D$ +67° (*c* 0.87, water). [Found: C, 28.64; H, 6.40; N, 10.75.] The hygroscopic hydrochloride, which gave positive reactions with ninhydrin and aniline acid phthalate,[4] sintered at 140° and darkened, but did not melt below 230°.[5]

Periodate oxidation of N,N′-dibenzoylneosaminol C (IV)[3a] gave N-benzoyl-L-serinaldehyde (negative rotation—*cf.* periodate oxidation of N-benzoyl-D-glucosaminol,[6] identified by papergrams after conversion to serine)[3] from C-1, C-2 and C-3 of neosamine C, while periodate oxidation of methyl N,N′-dibenzoylneobiosaminide C, (II), then bro-

(1) K. L. Rinehart, Jr., P. W. K. Woo, A. D. Argoudelis and A. M. Giesbrecht, THIS JOURNAL, **79**, 4567 (1957).

(2) K. L. Rinehart, Jr., P. W. K. Woo and A. D. Argoudelis, *ibid.*, **79**, 4568 (1957).

(3) K. L. Rinehart, Jr., and P. W. K. Woo, *ibid.*, **80**, 6463 (1958).

(3a) The compound numbers employed refer to formulas found in Neomycins III.[3]

(4) S. M. Partridge, *Nature*, **164**, 443 (1949).

(5) It has been reported [J. D. Dutcher, N. Hosansky, M. N. Donin and O. Wintersteiner, THIS JOURNAL, **73**, 1384 (1951)] that vigorous hydrochloric acid hydrolysis of methyl neobiosaminide C yielded the dihydrochloride of a reducing diamine, $[\alpha]^{22}D$ +69° (*c* 0.4 water) s. 155–175°, m.p. 182–185° dec. Analytical values of this material suggested the formula $C_8H_{14}N_2O_3{\cdot}2HCl$, that of a desoxydiaminohexose [however, *cf.* Ref. (1)].

(6) W. E. M. Lands, Ph.D. Thesis, University of Illinois, 1954.

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.

This investigation was supported in part by a research grant, No. E-1278, from the National Institute of Allergy and Infectious Diseases, Public Health Service. We also wish to express our thanks to the Upjohn Company for the generous gift of neomycin samples.

(7) K. Freudenberg, *Ber.*, **47**, 2027 (1914).

(8) P. W. Kent and M. W. Whitehouse, "Biochemistry of the Aminosugars," Butterworths Publications, Ltd., London, 1955, p. 202.

(9) E. E. van Tamelen, J. R. Dyer, H. E. Carter, J. V. Pierce and E. E. Daniels, THIS JOURNAL, **78**, 4817 (1956).

(10) Ref. (8), p. 171.

(11) "The Merck Index of Chemicals and Drugs," 6th ed., Merck and Co., Inc., Rahway, N. J., 1952, p. 34.

(12) C. S. Hudson, THIS JOURNAL, **31**, 66 (1909); **38**, 1566 (1916); **46**, 483 (1924).

(13) A. Neuberger and R. V. Pitt-Rivers, *Biochem. J.*, **33**, 1580 (1939); *cf.* also ref. (8), p. 59.

(14) S. A. Barker, E. J. Bourne, M. Stacey and D. H. Whiffen, *J. Chem. Soc.*, 171 (1954); S. A. Barker, E. J. Bourne and D. H. Whiffen, *Methods of Biochem. Anal.*, **3**, 213 (1956).

(15) A similar compound, $[\alpha]D$ +18°, has been obtained[M.-M. Janot, H. Pénau, D. Van Stolk, G. Hagemann and L. Pénasse, *Bull. soc. chim. France*, 1458 (1954)] as a degradation product of the antibiotic framycetin (Soframycin) by a procedure exactly paralleling that employed in the present studies. The nearly identical properties of this and other degradation products[14,16,18] of framycetin (hydrochloride: $[\alpha]D$ +57°) suggest its identity with neomycin B (hydrochloride: $[\alpha]D$ +63°,[16] +54°[18]).

(16) J. H. Ford, M. E. Bergy, A. A. Brooks, E. R. Garrett, J. Alberti, J. R. Dyer and H. E. Carter, THIS JOURNAL, **77**, 5311 (1955).

(17) R. Kuhn, *et al.*, *Angew. Chem.*, **69**, 23 (1957).

(18) (a) M. J. Cron, O. B. Fardig, D. L. Johnson, D. F. Whitehead, I. R. Hooper and R. U. Lemieux, THIS JOURNAL, **80**, 2342 (1958); (b) *ibid.*, **80**, 4741 (1958).

(19) O. K. Sebek, *J. Bacteriol.*, **75**, 199 (1958).

(20) Robert F. Carr Fellow, 1957–1958.

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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.

(2) D. J. Cram and H. Steinberg, THIS JOURNAL, **73**, 5691 (1951); D. J. Cram and N. L. Allinger, *ibid.*, **76**, 726, 2362 (1954); J. Abell and D. J. Cram, *ibid.*, **76**, 4406 (1954); D. J. Cram N. L. Allinger and H. Steinberg, *ibid.*, **76**, 6132 (1954); D. J. Cram and J. Abell, *ibid.*, **77**, 1179 (1955); D. J. Cram and R. W. Hierstod, *ibid.*, **77**, 1186 (1955); D. J. Cram and N. L. Allinger, *ibid.*, **77**, 6289 (1953); D. J. Cram and R. A. Reeves, *ibid.*, **80**, 3094 (1958); K. C. Dewhirst and D. J. Cram, *ibid.*, **80**, 3113 (1958).

(3) T. R. Tuttle, Jr., and S. I. Weissman, *ibid.*, **80**, 5342 (1958).