including diethyl 2,3-butadienylmalonate and 1-acetoxy-2,3-butadiene.

A more complete description of the synthesis of cyclobutanes from allenes and substituted olefins and the conversion of alkylidenecyclobutanes to cyclobutenes, alkylidenecyclobutenes and other dienes will be published shortly.

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KANAMYCIN. I. CHARACTERIZATION AND ACID HYDROLYSIS STUDIES

Sir:

Kanamycin, discovered by Umezawa and coworkers,[1] is a water-soluble basic antibiotic active on Mycobacteria, Gram-positive and Gram-negative organisms. It has been characterized as the base, the sulfate and other derivatives.[2]

Kanamycin is isolated from fermentation broths by adsorption on Amberlite IRC-50[3] resin in the sodium cycle and elution with aqueous hydrochloric acid. The eluate is neutralized, diluted and readsorbed on IRC-50 which has been regenerated with ammonium hydroxide. The column is eluted with 0.2 *N* NH_4OH, the eluate concentrated *in vacuo* to approximately 50–100 mg./ml. of kanamycin activity, diluted with 0.8–1 volume of methanol and adjusted with H_2SO_4 to *p*H 8.0–8.2. Kanamycin sulfate crystallizes slowly in small irregular pale yellow prismatic crystals.

The crystalline kanamycin sulfate may be purified by repeated recrystallization from methanol–water at *p*H 7.8–8.2 to give white irregular prismatic crystals. This preparation contains adsorbed moisture which is removed with difficulty. Samples for analytical determinations were dried to constant weight at 170° *in vacuo*. *Anal.* Calcd. for $C_{18}H_{36}N_4O_{11}\cdot H_2SO_4$: C, 37.13; H, 6.58; N, 9.62; S, 5.50; $SO_4^=$, 16.6; neut. eq., 145.6; mol. wt., 600.6 (monohydrate). Found: C, 37.3, 37.4, 37.3; H, 6.8, 6.6, 6.3; N, 9.3, 9.6; S, 5.5; $SO_4^=$, 16.8; neut. eq., 146.6; mol. wt. 604 (X-ray on undried material).[4] The formula containing two less hydrogen atoms, although improbable, is not excluded by analyses on this and other derivatives.

The sulfate is soluble in water, insoluble in the common alcohols and non-polar solvents. It shows no melting point, decomposing over a wide range above 250°. It was converted to kanamycin base by treatment of an aqueous solution with a strongly basic anion-exchange resin, concentration and crystallization with methanol–ethanol mixture, $[\alpha]^{24}D$ + 146 (*c* 1, 0.1 *N*, H_2SO_4). *Anal.* Calcd. for $C_{18}H_{36}N_4O_{11}$: C, 44.6; H, 7.5; N, 11.6; neut. eq., 121.1; mol. wt., 484.5. Found: C, 44.7, 45.0; H, 7.40, 7.6; N, 11.0, 11.5 (Dumas); 11.8, 11.8 (Van Slyke); neut. eq., 121.5; mol. wt. 468, 444 (Rast); 427, 490 (Signer). Kanamycin gives positive Molisch, ninhydrin and Elson–Morgan tests and negative reducing sugar, Sakaguchi and maltol tests. Treatment with 40% sulfuric acid for 100 min. at 100° yields a product with an ultraviolet spectrum identical to that obtained from a pentose under similar conditions.

Treatment of kanamycin base with acetic anhydride and methanol yields tetra-N-acetylkanamycin[2b] which was recrystallized from aqueous methanol, m.p. 250–255° dec. *Anal.* Calcd. for $C_{26}H_{44}N_4O_{15}$: C, 47.9; H, 6.8; N, 8.4. Found: C, 48.5; H, 6.90; N, 8.3. Kanamycin picrate was prepared by treating kanamycin base in water with picric acid. The product was recrystallized from boiling water, m.p. 225–230° with decomposition. *Anal.* Calcd. for $C_{42}H_{48}N_{16}O_{39}$: C, 36.0; H, 3.46. Found: C, 36.2, 36.2; H, 3.62, 3.60. Kanamycin also has been characterized by the formation of a series of Schiff bases. Treatment of kanamycin base in water with *p*-chlorobenzaldehyde in isopropyl alcohol yielded tetra-N-*p*-chlorobenzylidene kanamycin, m.p. 213–216° with decomposition. *Anal.* Calcd. for $C_{46}H_{48}Cl_4N_4O_{11}$: C, 56.7; H, 4.96; N, 5.75; mol. wt., 974. Found: C, 56.94, 56.74; H, 5.02, 4.73; N, 5.94, 5.73; mol. wt. 971 (Signer). In a similar fashion we have prepared the tetra-N-veratrylidene kanamycin, m.p. 173–175°. *Anal.* Calcd. for $C_{54}H_{68}N_4O_{19}$: C, 60.22; H, 6.32; N, 5.20. Found: C, 60.35; H, 6.28; N, 5.14. Tetra-N-salicylidene kanamycin melted at 272–274° with decomposition. *Anal.* Calcd. for $C_{46}H_{52}N_4O_{15}$: C, 61.33; H, 5.77. Found: C, 61.25; H, 5.75. Tetra-N-*p*-methoxybenzylidene kanamycin melted at 193–196° with decomposition. *Anal.* Calcd. for $C_{50}H_{60}N_4O_{15}$: C, 62.7; H, 6.27. Found: C, 62.6; H, 6.66.

Paper chromatography of kanamycin preparations revealed a second antibiotic, designated kanamycin B. The two antibiotics are best separated in Peterson's *n*-butanol–water–2% *p*-toluenesulfonic acid system[5] on Schleicher and Schuell 589 Blue Ribbon or Whatman No. 1 papers. In this system with S&S 589 Blue Paper, kanamycin has an R_F of about 0.35 and kanamycin B has an R_F of about 0.6. The presence of impurities or contaminating salts interferes markedly with the paper chromatography of the kanamycins in this system.

The infrared spectra of kanamycin and kanamycin B are similar. Each is typical of a polyhydroxy, polyamino compound. No carbonyl or carbon–carbon double bond adsorption is evident.

Kanamycin is remarkably resistant to acid and alkaline hydrolysis. Treatment of kanamycin with methanolic hydrogen chloride under conditions which hydrolyze neomycin B and C to neomycin A (neamine)[6–8] yielded unchanged starting material. Refluxing kanamycin base in 6 *N* HCl

(1) T. Takeuchi, T. Hikiji, K. Nitta, S. Yamazaki, S. Abe, H. Takayama and H. Umezawa, *J. Antibiotics*, **A10**, 107 (1957).

(2) (a) H. Umezawa, M. Ueda, K. Maeda, K. Yagishita, S. Kondo, Y. Okami, R. Utahara, Y. Osato, K. Nitta and T. Takeuchi, *ibid.*, **A10**, 181 (1957); (b) K. Maeda, M. Ueda, K. Yagishita, S. Kawaji, S. Kondo, M. Murase, T. Takeuchi, Y. Okami and H. Umezawa, *ibid.*, **A10**, 228 (1957).

(3) A product of the Rohm and Haas Co.

(4) The X-ray determination was run at the Massachusetts Institute of Technology, through the courtesy of Dr. David P. Shoemaker.

(5) D. H. Peterson and L. M. Reinecke, THIS JOURNAL, **72**, 3598 (1950).

(6) J. D. Dutcher, N. Hosansky, M. N. Donin and O. Wintersteiner, *ibid.*, **73**, 1384 (1951).

(7) B. E. Leach and C. M. Teeters, *ibid.*, **73**, 2794 (1951).

(8) R. L. Peck, C. E. Hoffhine, Jr., P. Gale and K. Folkers, *ibid.*, **75**, 1018 (1953).

for 45 min. completely destroyed the biological activity. After decolorizing, the solution was taken to a small volume and methanol and ethanol were added, yielding crystalline 1,3-diamino-4,5,6-trihydroxycyclohexane dihydrochloride (desoxystreptamine).[9] *Anal.* Calcd. for $C_6H_{14}N_2O_3 \cdot 2HCl$: C, 30.66; H, 6.86; N, 11.93; Cl, 30.17; neut. eq., 117.5. Found: C, 30.76; H, 6.99; N, 11.36; Cl, 29.6; neut. eq., 118.7. The compound showed no optical activity in acid or alkaline aqueous solution.

The dihydrochloride was converted to desoxystreptamine by dissolving in water, treating with Amberlite IR 410 ($O\bar{H}$),[3] concentrating, and crystallizing with ethanol. *Anal.* Calcd. for $C_6H_{14}N_2O_3$: C, 44.4; H, 8.70. Found: C, 44.66; H, 8.86.

A portion was converted to the dihydrobromide by crystallization from dilute aqueous HBr with methanol. It gave an infrared spectrum identical with that of an authentic sample of 1,3-diamino-4,5,6-trihydroxycyclohexane dihydrobromide isolated from neomycin.[10] The desoxystreptamine was additionally characterized by acetylation in pyridine and acetic anhydride to give pentaacetyl-1,3-diamino-4,5,6-trihydroxycyclohexane. *Anal.* Calcd. for $C_{16}H_{24}N_2O_8$: C, 51.6; H, 6.48; N, 7.53. Found: C, 51.7; H, 6.98; N, 7.30. Selective de-O-acetylation with Amberlite IR 410 ($O\bar{H}$)[3] in water yielded N,N′-diacetyl-1,3-diamino-4,5,6-trihydroxycyclohexane. *Anal.* Calcd. for $C_{10}H_{18}N_2O_5$: C, 48.77; H, 7.37. Found: C, 48.82; H, 7.73.

Other products of the acid hydrolysis shown to be present by paper chromatography include two ninhydrin-positive reducing materials, accounting for the major portion of the material left after removal of desoxystreptamine, and several minor components. These data allow speculation that kanamycin is a trisaccharide-like molecule, composed of two aminosugar moieties glycosidically linked to desoxystreptamine.

(9) D. A. Kuehl, Jr., M. N. Bishop and K. Folkers, THIS JOURNAL, **73**, 881(1951).

(10) Supplied by Dr. H. E. Carter, University of Illinois.

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THE RESOLUTION OF A HEXACOVALENT SILICON (IV) COMPLEX

Sir:

The possibility of six-coördinate silicon(IV) has been discussed by Stone and Seyferth[1] who described the availability of d-orbitals for bonding in silicon(IV) compounds. West[2] described the infrared spectra of $[Si(acac)_3]Cl \cdot HCl$ (I) and other β-diketones of silicon(IV), and from a comparison of these spectra with that of free acetylacetone concluded that the ligands of I behave as bidentate chelating agents.

(1) F. G. A. Stone and D. Seyferth, *J. Inorg. Nuclear Chem.*, 1, 112 (1955).

(2) R. West, Abstr. of Papers, 132nd Meeting, Am. Chem. Soc., 11-N (1957), THIS JOURNAL, in press.

Consequently, it appears highly probable that the cation of I should have an octahedral configuration,[3,4] which leads to the conclusion that it should be asymmetric. A resolution of racemic $[Si(acac)_3]^+$ into its optical enantiomers[5] would offer conclusive evidence for its octahedral configuration.

Optical Resolution Studies.—Racemic $[Si(acac)_3]Cl \cdot HCl$ was prepared by a modification of the method of Dilthey[6] and its resolution was attempted by treatment with sodium (−)-dibenzoyl-*d*-tartrate,[7-9] according to the equation[10]

$$2\text{D,L-}[Si(acac)_3]Cl \cdot HCl + d\text{-}(-)\text{-}Na_2C_{18}H_{12}O_8 \longrightarrow \text{L-}[Si(acac)_3]d\text{-}(-)\text{-}HC_{18}H_{12}O_8 + \text{D-}[Si(acac)_3]Cl \cdot HCl + 2NaCl \quad (1)$$

The diastereoisomer L-$[Si(acac)_3]d$-(−)-$HC_{18}H_{12}O_8$ is less soluble than the other diastereoisomer and precipitates from solution. For L-$[Si(acac)_3]$-*d*-(−)-$HC_{18}H_{12}O_8$, a 0.0088% solution showed α_{obs} to be $-0.068 \pm 0.003°$; $[\alpha]^{23}D$ −773°. The optical rotation of the diastereoisomer decreased (became more positive) with time as the asymmetric silicon complex ion racemized, and, after six hours, the observed rotation decayed to a constant value (−0.008°) due to the asymmetric monohydrogen dibenzoyl-*d*-(−)tartrate anion. In order to replace the resolving anion with chloride, the diastereoisomer was treated with an anion-exchange resin in the chloride form (Dowex 1-X8), which gave L-$[Si(acac)_3]Cl \cdot HCl$. A 0.0311% solution of this enantiomer showed α_{obs} to be $-0.300 \pm 0.003°$; $[\alpha]^{23}D$ −965°. The observed rotation decreased (became more positive) as the compound racemized, and decayed to zero degrees in six hours with a half-life of one hour. By extrapolation, the specific rotation, $[\alpha]^{23}D$ at zero time is found to be −1,300°. In order to determine whether the anion-exchange resin removed the negative rotating monohydrogen (−)-dibenzoyl-*d*-tartrate anion quantitatively from the diastereoisomer, an experiment was performed in which a sample of sodium monohydrogen (−)-dibenzoyl-D-tartrate was treated with resin under similar conditions; the filtrate showed no optical rotation, indicating that essentially complete removal of the asymmetric anion had been achieved.

The optical rotation of the filtrate from reaction 1 was found to be strongly dextrorotatory. It was treated with the chloride form of an anion-exchange resin (Dowex 1-X8) in order to remove the monohydrogen (−)-dibenzoyl-D-tartrate anion, and its rotation was measured. A 0.1164% solution showed $\alpha_{obs} = 0.790 \pm 0.03°$; $[\alpha]^{23}D$ +679°. The observed rotation of this solution of the *dex-*

(3) A. Werner, *Ber.*, **47**, 3087 (1914).

(4) J. C. Bailar, Jr., Ed., "Chemistry of the Coördination Compounds," Reinhold Publishing Co., New York, N. Y., 1956, pp. 274 ff.

(5) acac = acetylacetonate anion, $C_5H_7O_2^-$. This cation is also named tris-(2,4-pentanediono)-silicon(IV) cation.

(6) W. Dilthey, *Ber.*, **36**, 932, 1595 (1903).

(7) S. Kirschner, Dissertation, University of Illinois, 1954, p. 43.

(8) C. L. Butler and L. H. Cretcher, THIS JOURNAL, **55**, 2605 (1933).

(9) F. Zetzsche and M. Hubacher, *Helv. Chim. Acta*, **9**, 291 (1926).

(10) "D" and "L" indicate dextrorotatory and levorotatory complex ions, respectively; the "*d*-(−)-" prefix for dibenzoyltartrate indicates a negative rotating anion derived from dextrorotatory tartaric acid.