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Studies on Aminosugars. XXXII. Synthesis of 3′, 4′-Dideoxykanamycin B[1]

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Penta-*N*-ethoxycarbonylkanamycin B (**1**) prepared from kanamycin B was treated with 2,2-dimethoxypropane in DMF to give a 3′,4′;4″,6″-di-*O*-isopropylidene derivative (**3**). Subsequent benzoylation afforded a 2″-*O*-benzoyl derivative (**4**), Removal of the isopropylidene groups from **4** followed by controlled isopropylidenation afforded the corresponding 4″,6″-*O*-isopropylidene derivative (**5**), which was then transformed to a 3′,4′-di-*O*-mesyl derivative (**6**). Treatment of **6** with sodium iodide and zinc dust in DMF gave the desired 3′,4′-unsaturated derivative (**7**). Hydrogenation and removal of the protecting groups gave the title compound. The 3′,4′-dideoxykanamycin B expectedly showed remarkable activity against kanamycin-resistant bacteria as well as sensitive strains.

As described in the preceding papers, the 3′-deoxykanamycin[2] exhibited antibiotic activity in the same strength as the parent antibiotic and, moreover, it showed strong inhibition against resistant bacteria such as *E. coli* carrying R factor, resistant *Staphylococci* and *Pseudomonas*, whereas 3′-*O*-methylkanamycin[3] is inactive. On the other hand, we have found that 3,4-unsaturation of glycopyranosides smoothly proceeded by treatment of their 3,4-di-*O*-mesyl derivatives with iodide and zinc dust in dimethylformamide (DMF) as described in the foregoing paper.[4] The interest in this particular method of dehydroxylation is first that unsaturation occurs at C-3,4 position of an aminosugar and, fortunately, the yield of the reaction is excellent. Secondly, the reaction opens the possibility for us to synthesize a 3′,4′-dideoxy derivatives of kanamycin and allied antibiotics, though the structures of such antibiotics are much more complex. We were interested in the 3′,4′-dehydroxylation of kanamycin B because the antibiotic contains 2,6-diamino-2,6-dideoxy-D-glucose on which experience of 3,4-dehydroxylation has been gained.[4] Thus, the synthesis of 3′,4′-dideoxykanamycin B was undertaken.

The amino groups of kanamycin B were protected by ethoxycarbonyl chloride in aqueous acetone in the presence of sodium carbonate to give penta-*N*-ethoxycarbonylkanamycin B (**1**). The reason for the use of ethoxycarbonyl groups instead of benzyloxycarbonyl

1) A part of this paper was read by S. Umezawa at Symposium of New Natural Product Syntheses, 23rd International Congress of Pure and Applied Chemistry at Boston, U. S. A., July 28, 1971. Short communication: H. Umezawa, S. Umezawa, T. Tsuchiya, and Y. Okazaki, *J. Antibiot.* (Tokyo), **24**, 485 (1971).

2) S. Umezawa, T. Tsuchiya, R. Muto, Y. Nishimura, and H. Umezawa, *ibid* **24**, 274 (1971); S. Umezawa, Y. Nishimura, H. Hineno, K. Watanabe, S. Koike, T. Tsuchiya, and H. Umezawa, This Bulletin, **45**, 2847 (1972).

3) H. Umezawa, T. Tsuchiya, R. Muto, and S. Umezawa, *ibid.*, **45**, 2842 (1972).

4) S. Umezawa, T. Tsuchiya, and Y. Okazaki, *ibid.*, **44**, 3494 (1971); *ibid.*, **45**, 3619 (1972).

or acyl (acetyl or benzoyl) groups are that the benzyloxycarbonyl group seemed to have no special advantage over the ethoxycarbonyl group in the present synthesis and that the acyl protection of the amino groups in kanamycins renders the kanamycin-derivatives scarcely soluble in usual organic solvents. The product (**1**) was acetonated with 2,2-dimethoxypropane in DMF in the presence of *p*-toluenesulfonic acid giving 4″,6″-mono-*O*-isopropylidene derivative (**2**) in a yield of 95%. Its NMR spectrum in dimethyl sulfoxide-d_6 showed that the isopropylidene methyls resonated separately at τ 8.60 and 8.72, indicating[3] that the isopropylidene group was attached to C-4 and 6 of the 3-amino-3-deoxy-D-glucose moiety of the derivative (**2**). Compound **2** was again treated with 2,2-dimethoxypropane to give 3′,4′;4″6″-di-*O*-isopropylidene derivative (**3**), $[\alpha]_D^{20}+87°$ (*c* 1, DMF) in approximately 30% yield. Since the *N*-protected 4,5;4″,6″-di-*O*-isopropylidene derivative[3] of 6-*O*-(3-amino-3-deoxy-α-D-glucopyranosyl)-2-deoxystreptamine was obtained from the corresponding precursor in a yield of 84%, the above low yield may be ascribable to the molecular complexity of the kanamycin derivative (**2**). However, when dimethoxycyclohexane was used instead of dimethoxypropane and the reaction was performed under diminished pressure,[5] **1** gave the corresponding di-*O*-cyclohexylidene derivative in a high yield (90%), on which details will be published elswhere. Benzoylation of **3** gave 2″-*O*-benzoyl derivative (**4**), $[\alpha]_D^{21}+114°$ (*c* 1, DMF). Increase in optical rotation ($[\alpha]_D+87°$(in **3**)⟶$+114°$ (in **4**)) showed that the benzoylation occurred at the hydroxyl group on C-2″ but not on C-5 where is optically least sensitive and is sterically hindered. The inactivity of the hydroxyl group at C-5 to acylation was also encountered in the synthesis of kanamycin-6″-uronic acid.[6] Removal of the isopropylidene groups of **4** followed by controlled isopropylidenation gave the 2″-*O*-benzoyl-4″,6″-*O*-isopropylidene derivative (**5**) in a 73% yield. The positions selectively isopropylidenated were confirmed by its NMR spectrum.

Mesylation of **5** with mesyl chloride in pyridine gave the 3′,4′-di-*O*-mesyl derivative (**6**). 3′,4′-Unsaturation of **6** was performed by treatment[7] with sodium iodide and zinc dust in DMF as described in the previous paper.[4] 2″-*O*-Benzoyl-3′,4′-dideoxy-3′-eno-penta-*N*-ethoxycarbonyl-4″,6″-*O*-isopropylidenekanamycin B (**7**), $[\alpha]_D^{21}+36°$ (*c* 4, DMF), was obtained in a yield of 38%. Since methyl 2,6-di-*O*-benzoyl-3,4-dideoxy-α-D-*erythro*-hex-3-enopyranoside[4] (93%), methyl 2,3,4,6-tetradeoxy-2,6-dimethoxycarbonylamino-α-D-*erythro*-hex-3-enopyranoside[4] (90%) and 5,6-*O*-cyclohexylidene-3′,4′-dideoxy-3′-eno-tetra-*N*-methoxycarbonylneamine[8] (70%) were obtained from the corresponding precursors in high yields, the comparatively low

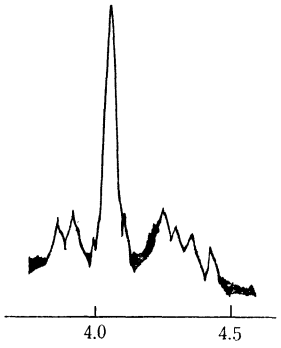

Fig. 1. The NMR spectrum of **7** in pyridine-d_5 at 60 MHz.

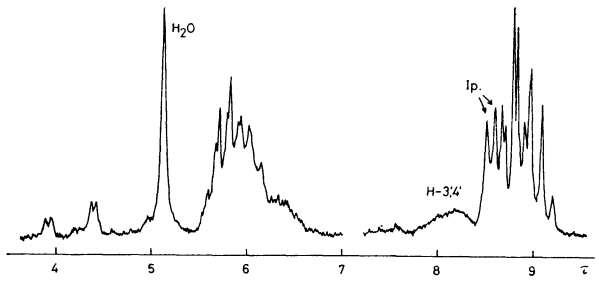

Fig. 2. The NMR Spectrum of **8** in pyridine-d_5 at 60 MHz.

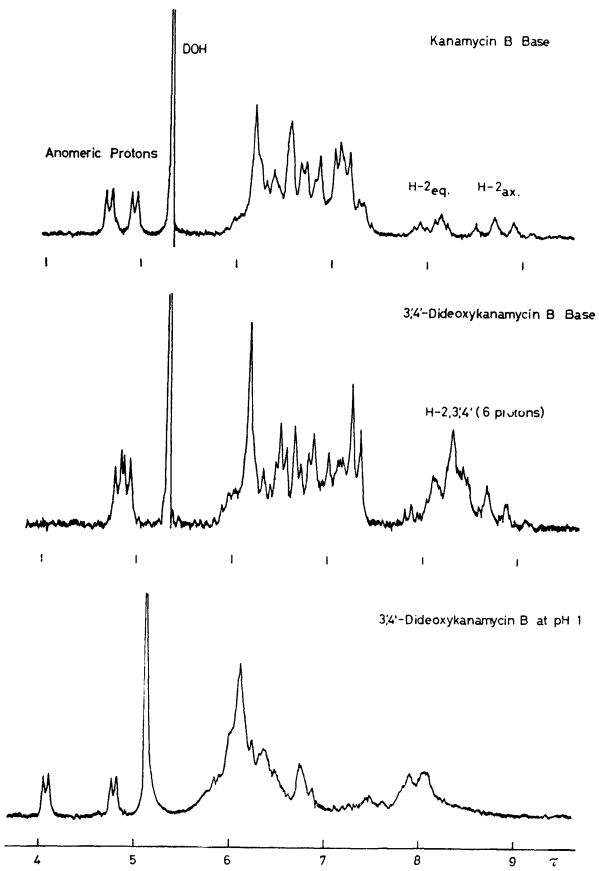

Fig. 3. The NMR spectra of kanamycin B base, 3′,4′-dideoxykanamycin B base and 3′,4′-dideoxykanamycin B at pH 1 (acidified with sulfuric acid) in D_2O at 60 MHz.

5) F. H. Bissett, M. E. Evans, and E. W. Parrish, *Carbohyd. Res.*, **5**, 184 (1967).
6) T. Kobayashi, T. Tsuchiya, K. Tatsuta, and S. Umezawa, *J. Antibiot.* (Tokyo), **23**, 226 (1970).
7) R. S. Tipson and A. Cohen, *Carbohyd. Res.*, **1**, 338 (1965).
8) S. Umezawa, T. Tsuchiya and T. Jikihara and H. Umezawa, *J. Antibiot.* (Tokyo), **24**, 711 (1971).

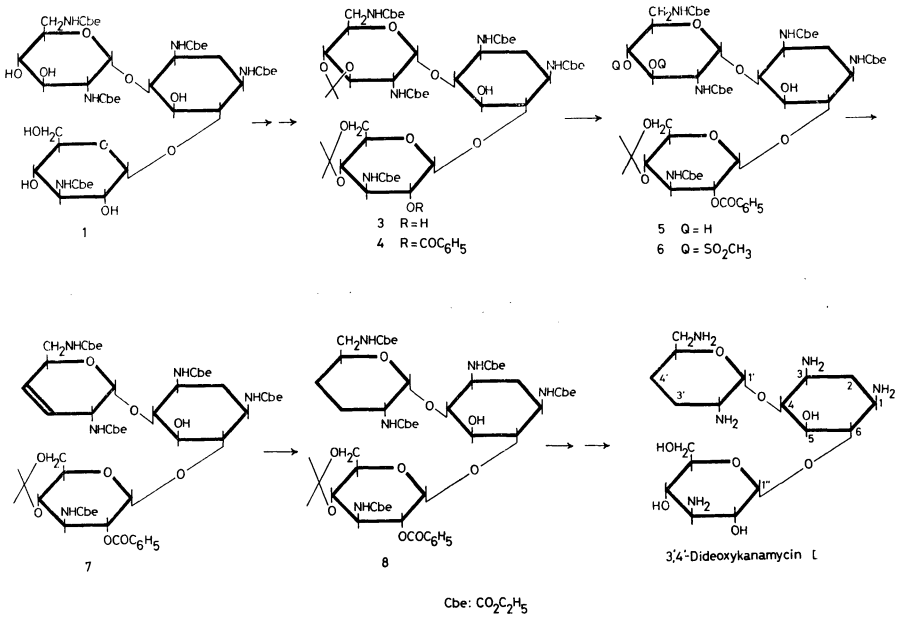

Chart 1.

yield of **7** may be due to some unfavorable influence of the free hydroxyl group of C-5 in **6**. 3',4'-Unsaturation of **7** was confirmed by its NMR spectrum (Fig. 1): a two proton singlet appeared at τ 4.04 characteristic to 3,4-alkene protons.[8] The low optical rotation (+36°) of **7** also required the above structure. As the hydrogenated product (**8**) described below had $[\alpha]_D$+93.5° (in DMF), the difference in molecular rotation between **7** and **8** is calculated to be (36—93.5°)×954 (MW of **7**)≃−55000°. The value, which will be the net contribution of the 3,4-unsaturation bond to the rotation of the α-D-*erythro*-hexopyranoside, is in good accord with that of structurally related compound **12** and **14** described in the preceding paper,[4] although methanol was used as the medium: (−35—126°)×274 (MW of **12**)≃−45000°.

Compound **7** was then catalytically hydrogenated to a dideoxy derivative (**8**), $[\alpha]_D^{22}$+93.5° (*c* 0.4 DMF). In the NMR spectrum (Fig. 2), a broadened signal corresponding to ethylene protons appeared (τ 7.8—8.5). Hydrolysis of **8** with aqueous acetic acid gave a deacetonation product (**9**), which, on removal of the other protecting groups with barium hydroxide, gave 3',4'-dideoxykanamycin B. The elemental analysis, the NMR spectrum (Fig. 3) and the result of hydrolysis of the product with 6 N hydrochloric acid confirmed the structure of the product as expected. It is worth describing that, in the NMR spectra, one of the doublets (J 3.5 Hz) of anomeric protons of 3',4'-dideoxykanamycin B base markedly shifts to down field (τ 4.80→4.08) on addition of sulfuric acid. The similar effect is also observed in the case of kanamycin B base (τ 4.66→4.12).

The semisynthetic 3',4'-dideoxykanamycin B exhibited the desired antibacterial spectrum. Microbiological studies[1] showed that resistant bacteria including various strains of *E. coli* carrying R factor, resistant *Staphylococci* isolated from patients, and *Pseudomonas aeruginisa* are remarkably sensitive to the antibiotic derivative.

Experimental

General. The general methods used were the same as those given in a previous paper.[4] Paper chromatography was performed on Toyo Roshi paper No. 50 with *n*-butanol-pyridine-water-acetic acid (6 : 4 : 3 : 1) and the spots were detected with 0.5% ninhydrin in pyridine and heating to 110°C. Frequently used solvent systems for TLC were as follows: benzene-methanol (4 : 1) (Solvent A) and chloroform-ethanol (12 : 1) (Solvent B).

*Penta-*N-*ethoxycarbonylkanamycin B (**1**).* To a mixture of kanamycin B base (1.0 g) and anhydrous sodium carbonate (0.9 g) in aqueous acetone (1 : 1, 20 m*l*), ethoxycarbonyl chloride (1.16 g) was added dropwise and the mixture was agitated for 1 hr at room temperature and then allowed to stand overnight. After the resulting slurry was neutralized with 1 N hydrochloric acid, the mixture was filtered, and the solid was washed with water, dried (1.46 g, 84%), and recrystallized from aqueous methanol (2 : 3), mp 304—306°C, $[\alpha]_D^{22}$+93.5° (*c* 0.3, DMF); R_f 0.34 (TLC with Solvent A); IR (KBr): 1700 (sh), 1690 (s), 1540 (s); 1040 (s), 975 (sh), 932 (w), 875 (m), 778 cm^{-1}. NMR (in dimethyl sulfoxide-d_6): τ 8.85 and 8.82 (each triplet, 15H in total, J 6.7 Hz, $NHCO_2CH_2\underline{CH_3}$).

Found: C, 47.03; H, 6.89; N, 8.32%. Calcd for $C_{33}H_{57}N_5O_{20}$: C, 46.97; H, 6.81; N, 8.30%.

*Penta-*N-*ethoxycarbonyl-4'',6''-*O-*isopropylidenekanamycin B (**2**).* To a mixture of **1** (1.05 g, 1.19 mmol) and anhydrous *p*-toluenesulfonic acid (29 mg, dried at 80°C *in vacuo*) in dry DMF (20 m*l* dried over CaH_2), 2,2-dimethoxypropane (0.43 g, 4.1 mmol) was added and the mixture was allowed to stand at 37°C for 1.5 hr. The starting material (R_f 0.29 on tlc with Solvent A) disappeared and the product (**2**, R_f 0.47) appeared with a slight amount of diisopropylidene product (**3**, R_f 0.76). A small amount of Amberlite IRA 400 (OH form) was added, and after filtration, the solution was concentrated *in vacuo* to a syrup, which was poured into water. The resulting solid was filtered and washed thoroughly with benzene, 1.05 g (95%). The solid was dissolved in dioxane and reprecipitated by the addition of water, mp>300°C,

$[\alpha]_D^{22}$+84° (*c* 0.5, DMF); IR (KBr): 1700 (s, broad), 1675 (sh), 1540; 1040 (broad), 945 (w), 907 (vw), 877, (w), 850 (w), 780 cm^{-1}.

Found: C, 48.62; H, 7.10; N, 8.02%. Calcd for $C_{36}H_{61}N_5O_{20}$: C, 48.92; H, 6.96; N, 7.92%.

NMR (in dimethyl sulfoxide-d_6): τ 8.84 (15H t, *J* 6.7 Hz, $NHCO_2CH_2C\underline{H}_3$), 8.72 and 8.60 (both 3H sinlgets, isopropylidene), 6.00 (10H q, *J* 6.7 Hz, $NHCO_2C\underline{H}_2CH_3$).

Penta-N-*ethoxycarbonyl-3′,4′;4″,6″-di*-O-*isopropylidenekanamycin B* (**3**). To a solution of **2** (13.7 g) and anhydrous *p*-toluenesulfonic acid (0.35 g) in dry DMF (70 ml), 2,2-dimethoxypropane (18.8 g) was added and the solution was heated at 65°C for 30 min. After concentration to approximately 60 ml, another 2,2-dimethoxypropane (35 g) and anhydrous *p*-toluenesulfonic acid (0.15 g) were added and the solution was again heated at 65°C for 30 min. After triethylamine (6 ml) was added, the solution was poured into a mixture of benzene (500 ml) and water (600 ml) with stirring. Resulting precipitates, which were suspended between aqueous and organic layers, were filtered, washed with benzene and dried to give a solid (6.5 g). This was proved to be the starting material unchanged (**2**, R_f 0.12 on tlc with Solvent B) and was again used in another run. The organic layer and the benzene washings were allowed to stand overnight, and some precipitates appeared were removed by filtration. The solution was evaporated to give solid (**3**), having an R_f 0.32 on tlc with Solvent B. The solid was dissolved in dioxane and reprecipitated by the addition of water, yielding 4.2 g (25.3%) of **3**, mp 236—237°C, $[\alpha]_D^{20}$ +87° (*c* 1, DMF); IR (KBr): 1735, 1705 (s), 1535; 1040, 1025, 985 (sh), 947 (w), 880 (w), 850 (w), 780 cm^{-1}.

Found: C, 50.54; H, 7.30; N, 7.59%. Calcd for $C_{39}H_{65}N_5O_{20}$: C, 50.70; H, 7.09; N, 7.58%.

NMR (in pyridine-d_5): τ 8.86 (15H t, *J* 6.7 Hz, $NHCO_2CH_2C\underline{H}_3$), 8.60 (12H a slightly broadened singlet, isopropylidene), 5.4—6.5 (27H multiplet, skeleton protons and $NHCO_2C\underline{H}_2$ CH_3).

2″-O-*Benzoyl-penta*-N-*ethoxycarbonyl-3′,4′;4″,6″-di*-O-*isopropylidenekanamycin B* (**4**). To a solution of **3** (3.24 g) in pyridine (48 ml), benzoyl chloride (1.68 g) was added and the solution was allowed to stand for 1 hr. After addition of water (0.4 ml), the solution was evaporated to give a syrup, which was dissolved in chloroform (200 mg). The solution was washed with sodium hydrogencarbonate solution and with water, dried over sodium sulfate and concentrated to approximately 20 ml. Addition of *n*-hexane (140 ml) to the solution gave a solid, 3.35 g (96%), mp 205—209°C, $[\alpha]_D^{21}$ +114° (*c* 1, DMF); IR (KBr): 1735—1700, 1535; 1030, 985 (sh), 950 (w), 877 (sh), 865 (w), 850 (w), 780, 715 cm^{-1}.

Found: C, 54.01; H, 7.11; N, 6.66%. Calcd for $C_{46}H_{69}N_5O_{21}$: C, 53.74; H, 6.77; N, 6.81%.

2″-O-*Benzoyl-penta*-N-*ethoxycarbonyl-4″,6″*-O-*isopropylidenekanamycin B* (**5**). A solution of **4** (282 mg) in aqueous acetic acid (1 : 3, 4 ml) was heated at 95°C for 1 hr. A deacetonated product (R_f 0.06 on tlc with Solvent B) appeared. The solution was coevaporated with toluene to give a solid, which was washed with water and dried (258 mg, 99%). To a solution of the deacetonated product (935 mg) in dry DMF (6 ml), 2,2-dimethoxypropane (230 ml) and anhydrous *p*-toluenesulfonic acid (20 mg) were added and the solution was allowed to stand at 30°C for 1 hr. On tlc with Solvent, B, a spot (R_f 0.36) appeared together with two minor spots of R_f 0.49 (**4**) and R_f 0.06. Another portion of 2,2-dimethoxypropane (96 mg) was added and the solution was allowed to stand for 1 hr at room temperature, the deacetonated substance (R_f 0.06) disappearing. Triethylamine (0.2 ml) was added and solution was poured into cold water (100 ml). The resulting precipitates were filtered, washed with water and dried. The solid, after washing with benzene, was dissolved in dioxane and reprecipitated by the addition of water, 722 mg (73% based on **4**), mp 305—307°C, $[\alpha]_D^{21}$ +105° (*c* 1, DMF); IR (KBr): 1735—1690, 1540; 1035, 985 (sh), 950 (w), 877 (w), 865 (w), 850 (w), 782, 713 cm^{-1}.

Found: C, 52.52; H, 6.67; N, 7.31%. Calcd for $C_{43}H_{65}N_5O_{21}$: C, 52.27; H, 6.63; N, 7.09%.

NMR (in dimethyl sulfoxide-d_6): τ 9.10, 8.86 and 8.83 (6H, 3H and 6H triplet, respectively, *J* 6.7 Hz, $NHCO_2CH_2C\underline{H}_3$), 8.70 and 8.56 (both 3H singlets, isopropylidene), 2.0—2.6 (5H multiplet, typical for benzoyl protons).

2″-O-*Benzoyl-penta*-N-*ethoxycarbonyl-4″,6″*-O-*isopropylidene-3′,4′-di*-O-*mesylkanamycin B* (**6**). To a solution of **5** (1.18 g) in pyridine (15 ml), methanesulfonyl chloride (0.56 g) was added and the solution was allowed to stand at room temperature for 1.5 hr. On tlc with chloroform–ethanol (12 : 1), a spot (R_f 0.30, mono-*O*-mesyl derivative) which appeared in an early stage of the reaction disappeared and a spot (R_f 0.35) appeared. After addition of water (0.1 ml), the solution was concentrated *in vacuo* to one-third volume and poured into water. Resulting precipitates were filtered, washed with water and dried yielding 1.32 g (96%), mp 198°C, $[\alpha]_D^{22}$ +107° (*c* 1.5, DMF); IR (KBr): 1735, 1720, 1700, 1540, 1350 (broad), 1175 (νSO_2); 1035, 965, 930 (sh), 877 (w), 865 (w), 850, 827, 782, 757 (w), 712 cm^{-1}.

Found: C, 47.36; H, 6.06; N, 5.38; S, 5.57%. Calcd for $C_{45}H_{69}N_5O_{25}S_2$: C, 47.24; H, 6.08; N, 6.12; S, 5.60%.

NMR (in pyridine-d_5): τ 8.95, 8.91 and 8.78 (3H, 6H and 6H triplet, respectively, *J* 6.7 Hz, $NHCO_2CH_2C\underline{H}_3$), 8.66 and 8.55 (both 3H singlets, isopropylidene).

2″-O-*Benzoyl-3′,4′-dideoxy-3′-eno-penta*-N-*ethoxycarbonyl-4″,6″*-O-*isopropylidenekanamycin B* (**7**). To a solution of **6** (100 mg) in dry DMF (2 ml), dry sodium iodide (1.1 g) and zinc dust (500 mg) were added and the mixture was heated in an oil bath (95±1°C) for 1 hr under vigorous stirring. A hot mixture of chloroform (10 ml) and water (10 ml) were added and, after stirring for a while, the mixture was filtered and the solid separated was washed with a mixture of chloroform–methanol (1 : 1, 2 ml×2). The filtrate and the washings were combined and the organic layer was washed successively with water, sodium thiosulfate solution and with water again, dried over sodium sulfate and evaporated to give a solid (94 mg). On tlc with benzene–ethyl acetate (1 : 3), the solid showed four spots of R_f 0.53 (**6**), 0.43 (**7**), 0.32 and 0.22 (major). The undesirable products (R_f 0.53, 0.32 and 0.22) were successfully removed from the solid by extraction with ethyl acetate several times. The residue (32 mg, 38%) was dissolved in a mixture of methanol (0.1 ml) and chloroform (0.2 ml) and to the solution, ethyl acetate (0.7 ml) was added. **7** gradually crystallized, mp 282—284°C, $[\alpha]_D^{21}$ +36° (*c* 4, DMF); IR (KBr): 1735, 1700 (s, sharp), 1540; 1040, 1030, 987, 950 (w), 925 (vw), 867 (w), 850 (w), 783, 745 (w), 714 cm^{-1}.

Found: C, 54.00; H, 6.71; N, 7.52%. Calcd for $C_{43}H_{63}N_5O_{19}$: C, 54.14; H, 6.66; N, 7.34%.

NMR (in pyridine-d_5): τ 8.97, 8.85, 8.81 and 8.78 (6H, 3H, 3H and 3H triplet, respectively, *J* 6.7 Hz, $NHCO_2CH_2C\underline{H}_3$), 8.56 and 8.51 (both 3H singlets, isopropylidene), 4.04 (2H s, H-3′,4′).

The major product (R_f 0.22) was proved not to be a deacetonation product of **7**; the structure is now under study.

2″-O-*Benzoyl-3′,4′-dideoxy-penta*-N-*ethoxycarbonyl-4″,6″*-O-*isopropylidenekanamycin B* (**8**). To a solution of **7** (115 mg) in a mixture of dioxane (4.5 ml), methanol (2.5 ml) and water (2.5 ml), platinum oxide (40 mg, preactivated with hydrogen) was added and the mixture was hydrogenated under

pressure (50 lbs/sq. inch) for 5 hr. The solution was filtered and the filtrate was evaporated to give a colorless solid (110 mg, 96%), which was dissolved in dioxane, and recrystallized by the addition of water, mp 271—272°C, $[\alpha]_D^{22}$ +93.5° (*c* 0.4, DMF).

Found: C, 54.15; H, 6.75; N, 7.64%. Calcd for $C_{43}H_{65}N_5O_{19}$: C, 54.02; H, 6.85; N, 7.33%.

NMR (in pyridine-d_5): τ 9.08, 8.97, 8.83 and 8.79 (3H, 3H, 3H and 6H triplet, respectively, *J* 6.7 Hz, $NHCO_2CH_2CH_3$), 8.60 and 8.51 (both 3H singlets, isopropylidene), 7.8—8.5 (~4H unresolved broadened signals, CH_2CH_2 at C-3′ and 4′), 5.5—6.5 (~24H m, skeleton protons and $NHCO_2CH_2CH_3$), 4.42 and 3.93 (each 1H d, *J* 3 Hz, H-1′, 1″).

*2″-O-Benzoyl-3′,4′-dideoxy-penta-N-ethoxycarbonylkanamycin B (**9**).* A solution of **8** (98 mg) in a mixture of water (0.5 m*l*) and acetic acid (0.8 m*l*) was heated in a boiling water bath for 5 min and the solution was allowed to stand at room temperature to give crystalline **9**. The mixture was stored in a refrigerator for several hours and the crystals were filtered, washed with cold water and dried to yield 73 mg (78%), mp 247—249°C, $[\alpha]_D^{24}$ +89° (*c* 2.7, DMF); IR (KBr): 1735 (sharp), 1700 (sharp), 1540; 1035, 1015 (sh), 990, 945 (w), 905 (w), 880 (w), 782, 720 cm^{-1}.

Found: C, 52.41; H, 6.54; N, 7.92%. Calcd for $C_{40}H_{61}N_5O_{19}$: C 52.45; H, 6.71; N, 7.65%.

*3′,4′-Dideoxykanamycin B (**10**).* A mixture of **9** (30 mg) and barium hydroxide octahydrate (250 mg) in aqueous dioxane (1 and 0.8 m*l*) was heated in a boiling water bath for 4.5 hr. Carbon dioxide was introduced, and the resulting suspension was heated for a while and centrifuged. The supernatant layer and the washings combined were evaporated to give a residue, which on paper chromatogram showed two spots of $R_{f\,\text{kanamycin B}}$ 1.3 (major, **10**) and 2 (minor); on tlc with the same solvent system, the residue also showed two spots of R_f 0.13 (major) and 0.26. The residue was charged on a column of Amberlite IRC-50 (NH_4 form) and, after washing with water, developed with 0.1—0.5 N ammonia with gradual increase of concentration. The minor substance (R_f 0.26 on tlc) was eluted with 0.3 N ammonia and the major with 0.5 N ammonia. The latter fraction was evaporated to give a solid, 9.6 mg (65%), $[\alpha]_D^{20}$ +132° (*c* 0.65, water).

Found: C, 48.05; H, 8.49; N, 15.54%. Calcd for $C_{18}H_{37}N_5O_8$: C, 47.88; H, 8.26; N, 15.51%.

Hydrolysis of 3′,4′-Dideoxykanamycin B. A solution of 3′,4′-dideoxykanamycin B in 6 N hydrochloric acid was heated at 95°C for 2 hr. Paper chromatogram of the resulting solution showed three spots of $R_{f\,\text{deoxystreptamine}}$ 1 (2-deoxystreptamine), 3 (3-amino-3-deoxy-D-glucose) and 2. The latest was assigned to be the spot of 2,6-diamino-2,3,4,6-tetradeoxyerythrose, which was obtained from the hydrolysis of methyl 2,6-diamino-2,3,4,6-tetradeoxy-α-D-erythropyranoside.[4]

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