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Deoxysugar Synthesis. I. Lithium-ethylamine Reduction of Carbohydrate Phosphorodiamidates

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Following the procedure of Ireland, *et al.*,[2] 3-phosphorodiamidates (**1b** and **6b**) of 1,2:5,6-di-O-isopropylidene-glucose and -allose were treated with lithium-ethylamine to give a 2,3-dideoxy compound (**3**) in good yield, while similar treatment of a glucosaminide 3-phosphorodiamidate (**11b**) yielded a 3-deoxy derivative (**12a**). Thus, this method has the advantage of convenience for the preparation of deoxysugars.

Ireland, *et al.*[2] recently reported an efficient method for deoxygenation of alcohols by means of a dissolving metal reduction of their N,N,N′,N′-tetramethylphosphorodiamidates (TMPDA). This reaction includes a direct reductive cleavage of alcoholic carbon-oxygen bond to give hydrocarbons in a way similar to the foregoing metal hydride reduction of their sulfonates which at present is still of limited use for deoxygenation. Therefore, it was of interest to investigate further aspects of this reaction using more complicated systems in which possible participation of neighboring groups exists. This paper deals with an extended application of Ireland's procedure for deoxygenation of alcohols to carbohydrate systems.

First, we investigated the 3-hydroxy function of 1,2: 5,6-di-O-isopropylidene-α-D-glucofuranose (**1a**) whose sulfonates are well-known to resist nucleophilic displacement.[3] Treatment of **1a** with a slight molar excess of sodium hydride and subsequently with N,N,N′,N′-tetramethylphosphorodiamidic chloride[4] (**2**) gave a phosphorodiamidate (**1b**) in good yield. Following the Ireland's procedure, reduction of **1b** was effected by treatment with lithium in ethylamine in the presence of *t*-butanol, giving an amine (**3**) which was almost homogeneous on its thin-layer chromatogram but was rather unstable, especially to acid. The infrared spectrum (IR) of the amine (**3**) showed absorption due to N-H at 3350 cm^{-1}. Its nuclear magnetic resonance spectrum (NMR) also suggested that one ethylamino group, one isopropylidene group and two methylenes are present in the structure of **3** and, in addition, it exhibited a notable signal at δ 4.77 ppm due to an anomeric proton. Based on these facts, the amine (**3**) was presumed to be a glycosylamine as shown in Chart 1.

Further, the presumed structure of the glycosylamine (**3**) was confirmed by the following transformations. Without purification, treatment of **3** with sodium borohydride in methanol gave a stable aminoalcohol (**4a**) which formed an N,O-diacetate on acetylation. Elementary analyses and NMR spectra of **4a** and **4b** reflected these structures, indicating that the aminoalcohol (**4a**) was formed by reduction of the potential imino group of **3**. In addition, the high resolution mass spectrum of the aminoalcohol (**4a**) revealed several main fragments as described in the experimental. The fragments at *m/e* 202 (M^+-CH_3) and *m/e* 159 ($M^+-CH_3COCH_3$) indicated the molecular formula of **4a**, and those at *m/e* 116 ($C_2H_5NHCH_2-CH_2-CH_2-CH=\overset{+}{O}H$

1) Location: *Hiromachi, 1-2-58, Shinagawa-ku, Tokyo.*
2) R.E. Ireland, D.C. Muchmore, and U. Hengartner, *J. Am. Chem. Soc.*, **94**, 5098 (1972).
3) *cf.* H. Schmidt and P. Karrer, *Helv. Chim. Acta*, **32**, 1371 (1949); M.L. Wolfrom, J. Bernsmann, and D. Horton, *J. Org. Chem.*, **27**, 4505 (1962).
4) H.G. Cook, J.D. Ilett, B.C. Saunders, G.J. Stacey, H.G. Watson, I.G. Wilding, and S.J. Woodcock, *J. Chem. Soc.*, **1949**, 2921.

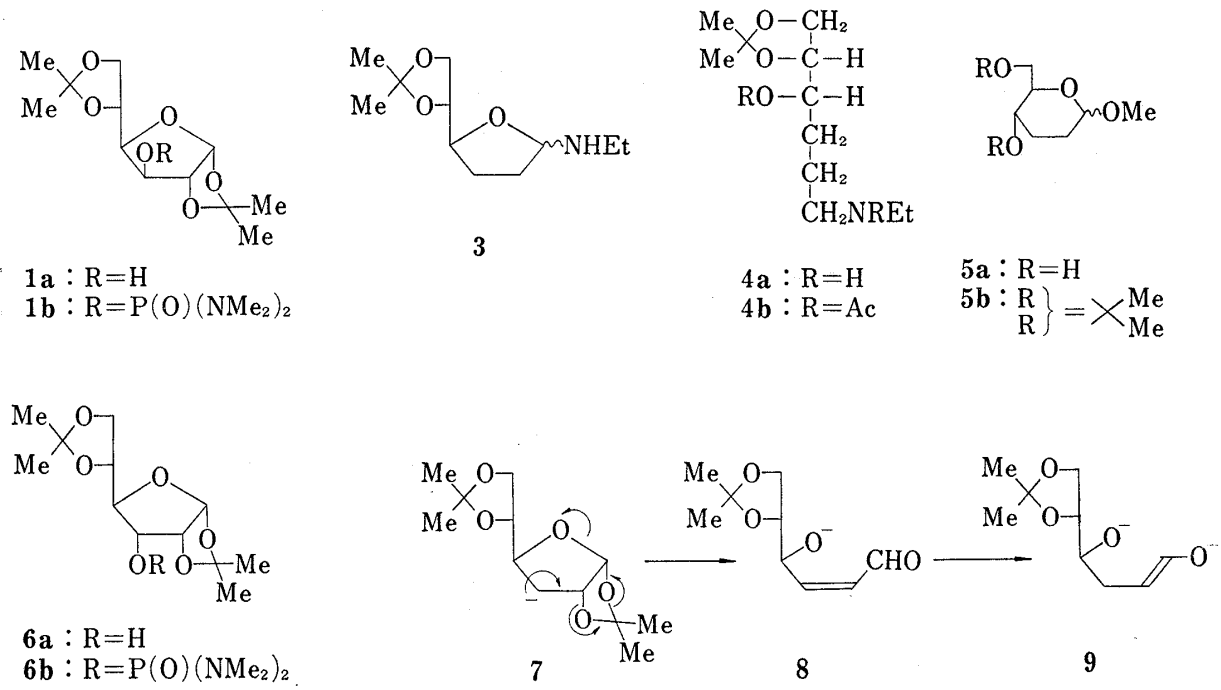


Chart 1

or its cyclized form) and *m/e* 71 (CH_2=$CHNHC_2H_5^+$) supported the presence of the chain of –CH(OH)–CH_2–CH_2–$CH_2NHC_2H_5$.

On the other hand, the glycosylamine (**3**) on warming in methanol in the presence of acid furnished an anomeric mixture of methyl pyranosides (**5a**) whose inertness to periodate oxidation excluded the furanoside structure. The pyranoside mixture was acetonated to give mono-O-isopropylidene derivatives (**5b**). Inevitably, these glycosides were methyl 2,3-dideoxy-D-*erythro*-hexopyranosides (**5a**) and their 4,6-O-isopropylidene derivatives (**5b**). Summarizing these facts, the glycosylamine structure (**3**) was assigned as N-ethyl-2,3-dideoxy-5,6-O-isopropylidene-D-*erythro*-hexofuranosylamine. Thus, it would appear that this lithium-ethylamine reduction of 3-phosphorodiamidates of 1,2-O-isopropylidene-furanoses might provide a new, interesting method for preparing several 2,3-dideoxy sugars, such as rhodinose, forosamine, and amicetose, which are important components of antibiotics.

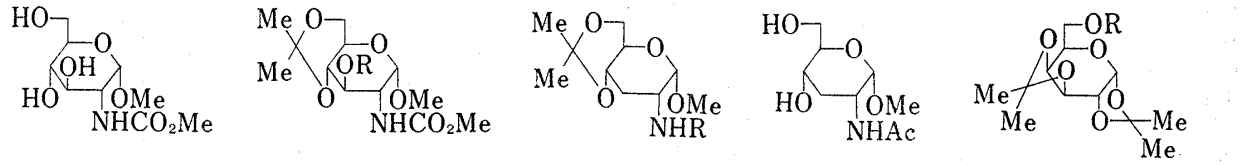
Analogous treatment of 1,2: 5,6-di-O-isopropylidene-α-D-allofuranose[5] (6a), the C_3-epimer of **1**, with the chloride (**2**) gave a syrupy phosphorodiamidate (**6b**). The reduction of **6b** with lithium-ethylamine proceeded in a similar way, giving the same glycosylamine (**3**). Based on this fact, formation of the dideoxy-furanosylamine (**3**) can be illustrated as the initial reductive cleavage of TMPDA group, successive removal of the isopropylidene group from the anion (**7**), which is formed from either phosphorodiamidate (**1b** and **6b**), and reduction of the resulting αβ-unsaturated aldehyde (**8**) to an enolate of saturated aldehyde (**9**) whose quenching followed by reaction with ethylamine solvent forms the glycosylamine (**3**).

Subsequently, this deoxygenation reaction was applied to the case of a glucosamine 3-hydroxy group as follows. Methyl 2-deoxy-2-methoxycarbonylamino-α-D-glucopyranoside[6] (**10**) was acetonated to give its 4,6-O-isopropylidene derivative (**11a**). A phosphorodiamidate (**11b**) analogously prepared from **11a** was reduced with lithium-ethylamine in the same way. Chromatographic separation of the reaction mixture gave a urethane (**12a**) in 43% yield and an amine (**12b**) in 29% yield. The NMR spectrum of the urethane (**12a**) exhibited signals corresponding to not only all protecting groups of the parent glucosaminide (**11a**) but also a newly

5) W. Sowa and G.H.S. Thomas, *Can. J. Chem.*, 44, 836 (1966).
6) D. Ikeda, T. Tsuchiya, and S. Umezawa, *Bull. Chem. Soc. Japan*, 44, 2529 (1971).

formed methylene group at δ 1.6—2.3 ppm, and, in addition, its mass spectrum showed a strong peak at *m/e* 260 (M^+-CH_3), indicating that the urethane (**12a**) is a 3-deoxy derivative of the parent glucosaminide (**11a**). The amine (**12b**) was treated with methyl chloroformate to give the urethane (**12a**) and, therefore, it was the deprotected derivative of **12a**. The deprotection of the amino group during the reaction could be deemed feasible by solvolysis of the urethane group in the presence of base.

Further, acetylation and successive deacetonation of the deoxyamine (**12b**) thus obtained gave methyl 2-acetamido-2,3-dideoxy-α-D-*ribo*-hexopyranoside (**13**) which proved identical with the authentic sample prepared by degradation of lividomycin.[7] Considering the hindered environment in the 3-hydroxy group of the protected glucosaminide (**11a**) wherein the nucleophilic displacement reaction *via* sulfonate has encountered some difficulties, it is expected that lithium-ethylamine reduction of phosphorodiamidates will furnish a versatile deoxygenation method in the carbohydrate field.



10 **11a** : R=H; **11b** : R=P(O)(NMe$_2$)$_2$ **12a** : R=CO$_2$Me; **12b** : R=H **13** **14a** : R=P(O)(NMe$_2$)$_2$; **14b** : R=H

Chart 2

Ireland, *et al.*[2] also described a successful example of the deoxygenation of an angular hydroxy methyl group into a methyl group in a fused cyclohexane ring. However, surprisingly enough, the reaction of a phosphorodiamidate (**14a**) derived from 1,2: 3,4-di-O-isopropylidene-α-D-galactopyranose (**14b**) by means of this procedure afforded the starting alcohol (**14b**) and the expected 6-deoxysugar was not detected at all. Supposedly, the possibility for solvolysis of the phosphorodiamidate (**14a**) during the reaction is remote; because, it was found that **14a** was stable and remained intact in a solution of lithium *t*-butoxide in ethylamine. The difference in the reaction pattern between these phosphorodiamidates of primary and secondary alcohols is not now comprehensible.

Experimental

Melting points are not corrected. IR spectra were recorded on a JASCO A-2 spectrometer, NMR spectra on a Varian A-60 or a Hitachi-Perkin Elmer R-24 spectrometer, and mass spectra (MS) on a JEOL JMS-OlSG mass spectrometer. Optical rotations were measured on a Perkin-Elmer Model 141 automatic polarimeter in 1 dm tubes. Thin-layer chromatography (TLC) was performed on TLC-plates, Silica gel F_{254} precoated, layer thickness 0.25 mm (E. Merck AG) and spots were visualized by spraying with vanadic acid-sulfuric acid reagent or with an ethanolic solution of phosphomolybdic acid. For column chromatography on silica gel, Wakogel C-200 (Wako Pure Chemical Industries, Ltd., Osaka, Japan) was used. Solvents were removed by a rotating flash evaporator at diminished pressures and usually at 35—50°.

1,2:5,6-Di-O-isopropylidene-α-D-glucofuranose 3-(N,N,N′,N′-Tetramethylphosphorodiamidate) (1b)—Sodium hydride (53% in mineral oil, 9.6 g) was washed twice with dry *n*-hexane and suspended in 180 ml of DMF and a solution of 26.0 g of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**1a**) in 60 ml of DMF was added dropwise with ice-cooling and stirring. After 30 min stirring, 25 g of N,N,N′,N′-tetramethylphosphorodiamidic chloride[4] (**2**) was added with ice-cooling. The reaction mixture was stirred for 30 min at 0° and poured onto ice-water and extracted with $CHCl_3$. The extract was dried and evaporated *in vacuo* to dryness and the crystalline residue was recrystallized from ether–hexane to afford 30 g of **1b** as needles, mp 101—102°, $[\alpha]_D^{21}$ −51.4° (*c*=1.35, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1222, 1070, 1018, 985. NMR ($CDCl_3$) δ ppm: 1.30 (6H, isopropylidene), 1.40, 1.49 (3H each, s, isopropylidene), 2.64, 2.70 (6H each, d, J=10 Hz, N–C$\underline{H}_3$), 4.67 (1H, br. d, J=6.5 Hz, C_3–H), 4.94 (1H, d, J=3.5 Hz, C_2–H), 5.90 (1H, d, J=3.5 Hz, C_1–H). *Anal.* Calcd. for $C_{16}H_{31}O_7N_2P$: C, 48.72; H, 7.92; N, 7.10. Found: C, 49.15; H, 7.97; N, 7.29.

7) T. Oda, T. Mori, and Y. Kyotani, *J. Antibiotics*, **24**, 503 (1971).

N-Ethyl-2,3-dideoxy-5,6-O-isopropylidene-D-*erythro*-hexofuranosylamine (3)——To a blue solution of 3.0 g of lithium in 80 ml of ethylamine was added slowly a mixture of 15.0 g of **1b**, 9.0 g of *t*-butanol, and 15 ml of tetrahydrofuran with cooling (ice-salt bath) and stirring under N_2 atmosphere. The blue color of the solution was maintained throughout the addition. After the addition was completed, the reaction mixture was stirred at below 0°. Excess lithium was removed and the reaction mixture was quenched with cold water and extracted three times with ether. The combined extract was washed H_2O, dried and evaporated to dryness, giving 7.4 g of an oil which was almost homogeneous by TLC. The analytical sample of 3 was obtained by vacuum distilation, bp 100—110° (1 mm Hg). IR $\nu_{max}^{liq.}$ 3350 cm^{-1}. NMR ($CDCl_3$) δ ppm: 1.09 (3H, t, J=7 Hz, N–CH_2–$C\underline{H}_3$), 1.33, 1.39 (3H each, s, isopropylidene), 1.6—2.3 (5H, m), 2.79 (2H, m, N–$C\underline{H}_2$–CH_3), 3.6—4.2 (4H, m), 4.77 (1H, m, C_1–H). *Anal.* Calcd. for $C_{11}H_{21}O_3N$: C, 61.36; H, 9.83; N, 6.51. Found: C, 61.39; H, 9.90; N, 6.94.

Analogously, treatment of the phosphorodiamidate (**6b**) of 1,2:5,6-di-O-isopropylidene-α-D-allofuranose was effected with lithium-ethylamine, giving **3** which proved identical with the sample obtained as above by TLC and IR spectrometry.

1,2,3-Trideoxy-1-ethylamino-5,6-O-isopropylidene-D-*erythro*-hexitol (4a) and Its Acetate (4b)——To a solution of 5.0 g of the crude **3** obtained above in 20 ml of methanol was added 1.0 g of sodium borohydride with ice-cooling and stirring. After stirring at room temperature for 1 hr, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The extract was washed with H_2O, dried and evaporated to a crystalline residue which was recrystallized from ether–hexane to give 3.9 g of **4a** as prisms, mp 87—88°, $[\alpha]_D^{21}$ *ca.* 0° (c=2.3, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3270, 3080 (br.). NMR ($CDCl_3$) δ ppm: 1.10 (3H, t, J=7 Hz, N–CH_2–$\underline{CH}_3$), 1.36, 1.39 (3H each, s, isopropylidene). Mass Spectrum *m/e*: 202.1425 ($M^+ - \cdot CH_3$, Calcd. 202.1443), 159.1227 ($M^+ - CH_3COCH_3$, Calcd. 159.1259), 142.1178 ($M^+ - \cdot CH_3$–AcOH, Calcd. 142.1231), 141.1118 ($M^+ - CH_3COCH_3 - H_2O$, Calcd. 141.1153), 116.1058 [$M^+ - \cdot C_5H_9O_2$ (C-5,6 unit), Calcd. 116.1075], 98.0982 ($M^+ - C_5H_9O_2 - H_2O$, Calcd. 98.0969), 71.0736 [$M^+ - C_7H_{14}O_3$ (C-3,4,5,6 unit), Calcd. 71.0734]. *Anal.* Calcd. for $C_{11}H_{23}O_3N$: C, 60.80; H, 10.67; N, 6.47. Found: C, 60.97; H, 10.66; N, 6.64.

Acetylation of 300 mg of **4a** with 0.5 g of Ac_2O and 2 ml of pyridine gave 203 mg of the acetate (**4b**) as a syrup, bp 180—190° (1 mmHg, bath temp.). IR $\nu_{max}^{liq.}$ cm^{-1}: 1740, 1640. NMR ($CDCl_3$) δ ppm: 1.09 and 1.15 (3H, t, *ca.* 1:2, N–CH_2–$C\underline{H}_3$), 1.33, 1.38 (3H each, isopropylidene), 2.05 (6H, s, two acetyl). 3.0—3.5 (4H, m, –$C\underline{H}_2$–N–$C\underline{H}_2$–), 3.7—4.3 (3H, m, –CH_2–O– and –$\underline{C}H$–O–), 4.97 (1H, m, –$\underline{C}H$OAc). *Anal.* Calcd. for $C_{15}H_{27}O_5N$: C, 59.78; H, 9.03; N, 4.65. Found: C, 59.34; H, 8.75; N, 5.09.

Methyl 2,3-Dideoxy-D-*erythro*-hexopyranoside (5a) and Its 4,6-O-Isopropylidene Derivative (5b)——A solution of 2.5 g of the crude **3** in 60 ml 20% methanolic HCl was refluxed overnight. The solution was neutralized with basic lead carbonate and filtered. The filtrate was evaporated to leave anoil whose TLC showed two spots corresponding to the α- and β-anomers. The oil thus obtained was chromatographed on a column of silica gel (25 g) using AcOEt as eluant to give 0.6 g of **5a** as a syrup. IR $\nu_{max}^{liq.}$ 3400 cm^{-1}. NMR ($CDCl_3$) δ ppm: 1.6—2.1 (4H, m, –$(CH_2)_2$–), 3.31 (3H, s, OCH_3), 4.61 and 4.91 (1H, br. s and m, *ca.* 1:1, C_1–H). Mass Spectrum *m/e*: 131 ($M^+ - OCH_3$), 113 (131–H_2O). *Anal.* Calcd for $C_7H_{14}O_4$: C, 51.84; H, 8.70. Found: C, 51.23; H, 8.69.

This anomeric mixture (**5a**) was not oxidized by sodium periodate in H_2O.

Acetonation of **5a** with 2,2-dimethoxypropane in DMF in the presence of a small amount of TsOH at room temperature gave the 4,6-O-isopropylidene derivative (**5b**) as an oil, bp 90—100° (1 mmHg, bath temp.). NMR ($CDCl_3$) δ ppm: 1.30, 1.34 (3H each, s, isopropyridene), 1.6—2.1 (4H, m, –$(CH_2)_2$–), 3.22 and 3.28 (3H, s, *ca.* 1:1, OCH_3), 3.5—4.1 (4H, m), 4.56 and 4.91 (1H, br. s and m, *ca.* 1:1, C_1–H). Mass Spectrum *m/e*: 187 ($M^+ - CH_3$), 171 ($M^+ - OCH_3$), 127 ($M^+ - CH_3 - CH_3COOH$). *Anal.* Calcd. for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 58.77; H, 8.94.

1,2:5,6-Di-O-isopropylidene-α-D-allofuranose 3-(N,N,N′,N′-Tetramethylphosphorodiamidate) (6b)——Sodium hydride (53% in mineral oil, 0.60 g) was washed twice with dry *n*-hexane and suspended in 25 ml of dry tetrahydrofuran and a solution of 2.60 g of 1,2:5,6-di-O-isopropylidene-α-D-allofuranose[5] (**6a**) in 10 ml of tetrahydrofuran was added dropwise with stirring. After stirring for 15 min, 2.0 g of **2** was added with ice-cooling and stirring. The reaction mixture was worked up as described before and the product was purified by silica gel chromatography, giving 3.0 g **6b** as a syrup, $[\alpha]_D^{21}$ +66.5° (c=1.73, $CHCl_3$). IR $\nu_{max}^{liq.}$ cm^{-1}: 1218, 1063, 1018, 998. NMR ($CDCl_3$) δ ppm: 1.24 (6H, s, isopropylidene), 1.34, 1.45 (3H each, s, isopropylidene), 2.55 (12H, d, J=10 Hz, N–CH_3), 4.61 (1H, t, J=3.5 Hz, C_2–H), 5.61 (1H, d, J=3.5 Hz, C_1–H). *Anal.* Calcd. for $C_{16}H_{31}O_7N_2P$: C, 48.72; H, 7.92; N, 7.10. Found: C, 48.45; H, 7.89; N, 6.88.

Methyl 2-Deoxy-4,6-O-isopropylidene-2-methoxycarbonylamino-α-D-glucopyranoside (11a) and Its 3-(N,N,N′,N′-Tetramethylphosphorodiamidate) (11b)——A solution of 13 g of methyl 2-deoxy-2-methoxycarbonylamino-α-D-glucopyranoside[6] (**10**), 2,2-dimethoxypropane, and 100 mg of TsOH·H_2O in 80 ml of DMF was allowed to stand overnight at room temperature and, then, heated on a steam bath for 30 min. After being cooled and neutralized with solid K_2CO_3, the mixture was filtered and the filtrate was evaporated *in vacuo* to a thick syrup which was dissolved in AcOEt, washed with H_2O, dried and evaporated, leaving 14.5 g of **11a** as a thick syrup. IR ν_{max}^{Nujol} cm^{-1}: 3450, 3325. NMR ($CDCl_3$) δ ppm: 1.43, 1.55 (3H each, s, isopropylidene), 3.37 (3H, s, OCH_3), 3.70 (3H, s, $COOCH_3$), 4.72 (1H, d, J=3 Hz, C_1–H), 5.37 (1H, d, J=8 Hz, NH).

To a suspension prepared from sodium hydride (53% in mineral oil, 2.0 g) in 60 ml of DMF, was added a solution of 8.0 g of **11a** in 10 ml of DMF and then 8.0 g of **2** with cooling and stirring. The reaction mixture was worked up as described before and the product was purified by silica gel chromatography, giving 8.7 g of **11b** as a syrup. IR $\nu_{max}^{liq.}$ cm^{-1}: 3300, 1729. NMR ($CDCl_3$) δ ppm: 1.37, 1.47 (3H each, s, isopropylidene), 2.54, 2.64 (6H each, d, $J=10$ Hz, N–CH_3), 3.33 (3H, s, OCH_3), 3.64 (3H, s, $COOCH_3$), 4.82 (1H, d, $J=4$ Hz, C_1–H), 6.15 (1H, br. d, $J=8$ Hz, NH). *Anal.* Calcd. for $C_{16}H_{32}O_8N_3P$: C, 45.17; H, 7.58; N, 9.88. Found: C, 45.01; H, 7.69; N, 9.08.

Methyl 2,3-Dideoxy-4,6-O-isopropylidene-2-methoxycarbonylamino-α-D-*ribo*-hexopyranoside (12a) and Methyl 2-Amino-2,3-dideoxy-4,6-O-isopropylidene-α-D-*ribo*-hexopyranoside (12b)——To a blue solution of 0.28 g of lithium in 30 ml of ethylamine was added 15 ml of tetrahydrofuran with cooling (ice-salt) and stirring under N_2 atmosphere. Then, a solution of 1.70 g of **11b** and 0.9 g of *t*-butanol in 15 ml of tetrahydrofuran was added slowly as described earlier. The reaction mixture was stirred for 30 min with ice-cooling and quenched with H_2O, and extracted with $CHCl_3$. The extract was dried and evaporated to give 0.85 g of a syrup which was chromatographed on silica gel. Elution with benzene–AcOEt (1:1, v/v) followed by evaporation gave 0.47 g (43%) of **12a** as a syrup, $[\alpha]_D^{20}+80.1°$ ($c=1.9$, $CHCl_3$). IR $\nu_{max}^{liq.}$ cm^{-1}: 3350, 1725. NMR ($CDCl_3$) δ ppm: 1.39, 1.49 (3H each, s, isopropylidene), 1.6—2.3 (2H, m, $-CH_2-$), 3.37, s, OCH_3), 3.66 (3H, s, $COOCH_3$), 4.58 (1H, d, $J=4$ Hz, C_1–H), 4.91 (1H, br. d, $J=9$ Hz, NH). Mass Spectrum *m/e*: 275 (M^+, weak), 260 (M^+-CH_3). *Anal.* Calcd. for $C_{12}H_{21}O_6N$: C, 52.35; H, 7.69; N, 5.09. Found: C, 52.62; H, 7.79; N, 4.86.

Successively, elution with AcOEt–MeOH (20:1, v/v) followed by evaporation gave 0.25 g (29%) of **12b** as a syrup. IR $\nu_{max}^{liq.}$ cm^{-1}: 3400, 3320. NMR ($CDCl_3$) δ ppm: 1.34, 1.43 (3H each, s, isopropylidene), 3.32 (3H, s, OCH_3), 4.46 (1H, d, $J=4$ Hz, C_1–H).

The amine (**12b**, 100 mg) was treated with 100 mg of methyl chloroformate and 30 mg of K_2CO_3 in 2 ml of acetone at room temperature for 1 hr. The reaction mixture was worked up in the usual manner and the product was isolated as a syrup which was identified with the sample of **12a** obtained above by IR and NMR spectra and TLC.

Methyl 2-Acetamido-2,3-dideoxy-α-D-*ribo*-hexopyranoside (13)——A mixture of 290 mg of **12b**, 0.3 ml of Ac_2O, and 2 ml of pyridine was heated on a stream bath for 5 min. The reaction mixture was treated with H_2O and extracted with ether. The extract was washed with H_2O, dried and evaporated to dryness. The residue was purified by silica gel chromatography, yielding 305 mg of an isopropylidene derivative of **13** as a colorless syrup, $[\alpha]_D^{20}+81.2°$ ($c=2.33$, $CHCl_3$). IR $\nu_{max}^{liq.}$ cm^{-1}: 3300, 1652. NMR ($CDCl_3$) δ ppm: 1.31, 1.40 (3H each, s, isopropylidene), 1.89 (3H, s, N–$COCH_3$), 3.30 (3H, s, OCH_3), 4.49 (1H, d, $J=3.5$ Hz, C_1–H), 5.75 (1H, br. d, $J=8$ Hz, NH). *Anal.* Calcd. for $C_{12}H_{21}O_5N$: C, 55.58; H, 8.16; N, 5.40. Found: C, 55.86; H, 8.50; N, 5.20.

The isopropylidene derivative (150 mg) thus obtained was treated with 2 ml of MeOH containing 3 mg of $TsOH\cdot H_2O$ at room temperature and neutralized with Amberlite IR-45 (OH^-). Removal of the solvent gave a crystalline residue which was recrystallized from AcOEt–MeOH to give 102 mg of **13**, mp 210—213°, $[\alpha]_D^{20}+131°$ ($c=0.56$, H_2O) (lit.[7] mp 206—209°, $[\alpha]_D^{20}+112.2°$). The product was identified with the sample obtained by degradation of lividomycin[7] by IR spectrometry. IR ν_{max}^{Nujol} cm^{-1}: 3310, 1641, 1541. NMR (DMSO-d_6) δ ppm: 1.76 (3H, s, N–$COCH_3$), 3.22 (3H, s, OCH_3), 4.46 (1H, d, $J=4$ Hz, C_1–H), 7.68 (1H, br. d, $J=8$ Hz, NH).

1,2:3,4-Di-O-isopropylidene-α-D-galactopyranose 6-(N,N,N′,N′-Tetramethylphosphorodiamidate) (14a) and Its Reaction with Lithium-ethylamine——A solution of 5.2 g of 1,2:3,4-di-O-isopropylidene-α-D-galactopyranose[8] (**14b**) and 5.2 g of **2** in 30 ml of pyridine was warmed at 80—90° for 2 hr. The cooled mixture was poured onto ice-water and extracted with $CHCl_3$. The extract was washed with H_2O, dried and evaporated *in vacuo*, leaving 5.2 g of a crystalline residue which was recrystallized from ether–hexane to give 5.2 g of **14a** as prisms, mp 67—70°, $[\alpha]_D^{20}-36.7°$ ($c=1.15$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1217, 1068, 999. NMR ($CDCl_3$) δ ppm: 1.32 (6H, s, isopropylidene), 1.44, 1.55 (3H each, s, isopropylidene), 2.66 (12H, d, $J=10$ Hz, N–CH_3), 4.34 (1H, dd, $J=5$ and 2.5 Hz, C_2–H), 4.65 (1H, dd, $J=8$ and 2.5 Hz, C_3–H), 5.57 (1H, d, $J=8$ Hz, C_1–H). *Anal.* Calcd. for $C_{16}H_{31}O_7N_2P$: C, 48.72; N, 7.10. Found: C, 48.67; H, 7.87; N, 7.90.

To a blue solution of 0.7 g of lithium in 30 ml of ethylamine was added dropwise a solution of 3.50 g of **14a** and 2.2 g of *t*-butanol in 10 ml of tetrahydrofuran with cooling and stirring as described earlier. After 30 min stirring, excess lithium was removed and the reaction mixture was quenched with H_2O and extracted with $CHCl_3$. The extract was dried and evaporated, giving 1.5 g of a syrup which was chromatographed on silica gel. Elution with benzene–ether (1:1, v/v) gave 1.0 g of **14b** as a syrup which was identified with the authentic sample by IR and NMR spectra and TLC.

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8) R.L. Whistler and M.L. Wolfrom (ed.), "Methods in Carbohydrate Chemistry," Vol. II, Academic Press, Inc., N.Y. & London, 1963, p. 247.