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Note

Tetrafluoroboric acid, an efficient catalyst in carbohydrate protection and deprotection reactions

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Initiated by discussions on the mechanism of acetal cleavage by lithium tetrafluoroborate in wet acetonitrile[1] (which we had successfully applied to a carbohydrate educt[2]), a series of experiments was started in order to elucidate the catalyzing potency of tetrafluoroboric acid itself; we now report some of the results obtained from the application of either its ethereal or its aqueous solution to simple carbohydrate reactions.

Independent of the structure of the educt, as well as of the nature of the protecting group present, ethereal tetrafluoroboric acid readily catalyzes transacetalation reactions[3]; the best results (82–97% yield within 1 to 4 h at room temperature) were obtained in *N,N*-dimethylformamide, using equimolar amounts of tetrafluoroboric acid (see entries 1–5, Table I). From these reactions, selective formation of the monoacetal **6** (ref. 4) from methyl α-D-mannopyranoside (**5**) is of special interest.

Ethereal tetrafluoroboric acid also promotes direct isopropylidenation (see entries 6 and 7, Table I); thus, from the reaction of D-glucose and acetone (in the presence of molecular sieve 4A) 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[5] (**20**) is obtained in 85% yield after 0.5 h at 50°.

Interesting "deprotecting properties" were displayed by aqueous tetrafluoroboric acid[6], which, in acetonitrile, cleaved acetals (see entries 1–5, Table II), trityl ethers (entries 6 and 7) — also both simultaneously (entry 9) — as well as *tert*-butyldimethylsilyl ethers (entry 8) within minutes at room temperature; *tert*-butoxycarbonyl groups, slightly affected under the latter conditions, are quickly removed by neat aqueous tetrafluoroboric acid (see entry 11, Table II).

By stepwise addition of the catalyst to a solution of **20** in 1:1 acetone–water, selective removal of the 5,6-*O*-isopropylidene group is achieved, thus allowing the isolation of 1,2-*O*-isopropylidene-α-D-glucofuranose[5] (**35**) in 96% yield (see entry 10).

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TABLE I

TRANSFORMATIONS CATALYZED BY ETHEREAL TETRAFLUOROBORIC ACID

Entry	*Educt*	*Reagent and conditions*	*Time (h)*	*Product*	*Yield (%)*
1	Methyl α-D-gluco- (**1**), α-D-galacto-[9] (**3**), and α-D-manno-pyranoside[4] (**5**)	benzaldehyde dimethyl acetal[3], $HCONMe_2$, 20°	1 (**1**) 4 (**3**) 3 (**5**)	methyl 4,6-*O*-benzylidene-α-D-gluco-[3] (**2**), -α-D-galacto-[9] (**4**), and -α-D-manno-pyranoside[4] (**6**)	97.2 (**2**) 96.4 (**4**) 93.7 (**6**)
2	Benzyl 2-benzamido-2-deoxy-α-D-glucopyranoside[10] (**7**)		1	benzyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (**8**)	93.8
3	Methyl 3-(*tert*-butoxycarbonyl)-amino-3-deoxy-α-D- (**9**) and -β-D-glucopyranoside[11] (**11**)		3	methyl 4,6-*O*-benzylidene-3-(*tert*-butoxycarbonyl)amino-3-deoxy-α-D- (**10**) and -β-D-glucopyranoside (**12**)	85.8 (**10**) 78.7 (**12**)
4	1,2-*O*-Isopropylidene-6-*O*-trityl-α-D-glucofuranose[12] (**13**)		1	3,5-*O*-benzylidene-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-glucofuranose[12] (**14**)	82.5
5	Tetra-*N*-(benzyloxycarbonyl)-kanamycin A (ref. 13, **15**)	cyclohexanone dimethyl acetal[14], $HCONMe_2$, 20°	2	tetra-*N*-(benzyloxycarbonyl)-4″,6″-*O*-cyclohexylidenekanamycin A (ref. 13, **16**)	91.7
6	D-Glucofuranurono-6,3-lactone (**17**)	acetone, 20°	0.3	1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone[15] (**18**)	89.1
7	D-Glucose (**19**)	acetone, 50°	0.5	1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[5] (**20**)	85.4

TABLE II

TRANSFORMATIONS CATALYZED BY AQUEOUS TETRAFLUOROBORIC ACID

Entry	*Educt*	*Conditions*	*Time (h)*	*Product*	*Yield (%)*
1	**2, 4, 6, 8, 20**	acetonitrile 20°	0.2	**1, 3, 5, 7, 19**	90.8 (**1**) 87.2 (**3**) 94 4 (**5**) 93 9 (**7**) [a] (**19**)
2	Methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-brosyl-α-D-allopyranoside (**21**)		0 2	methyl 2-*O*-benzoyl-3-*O*-brosyl-α-D-allopyranoside (**22**)	91.5
3	Methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-*ribo*-hexopyranosid-3-ulose[16] (**23**)		0 2	methyl 2-*O*-benzoyl-α-D-*ribo*-hexopyranosid-3-ulose (**24**)	93 5
4	Methyl 4,6-*O*-benzylidene-2,3-di-*O*-tosyl-α-D-glucopyranoside[17] (**25**)		0 5	methyl 2,3-di-*O*-tosyl-α-D-glucopyranoside (**26**)	98.7
5	2′,3′,4′,2″-Tetra-*O*-benzoyltetra-*N*-(benzyloxycarbonyl)-4″,6″-*O*-cyclohexylidenekanamycin A (ref 13, **27**)		0 5	2′,3′,4′,2″-tetra-*O*-benzoyl-tetra-*N*-(benzyloxycarbonyl)-kanamycin A (**28**)	92 5
6	Methyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside[18] (**29**)		0.5	methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside[19] (**30**)	93 6
7	Benzyl 3,4-di-*O*-acetyl-2-benzamido-2-deoxy-6-*O*-trityl-α-D-gluco-pyranoside[7] (**31**)		0 2	benzyl 3,4-di-*O*-acetyl-2-benzamido-2-deoxy-α-D-gluco-pyranoside[7] (**32**)	94 6
8	Methyl 6-(benzyloxycarbonyl)amino-2-*O*-(*tert*-butyldimethylsilyl)-6-deoxy-α-D-glucopyranoside (**33**)		0 2	methyl 6-(benzyloxycarbonyl)-amino-6-deoxy-α-D-gluco-pyranoside (**34**)	94 5
9	**13, 14**		0 2	**19**	[a]
10	**20**	acetone–H_2O 20°[b]	5	1,2-*O*-isopropylidene-α-D-glucofuranose[5] (**35**)	96 2
11	Tetra-*N*-(*tert*-butoxycarbonyl)-kanamycin A (ref 11, **36**)	20°[c]	0 1	kanamycin A[d] (**37**)	[a]

[a]Not determined. [b]Stepwise addition of the catalyst, with t.l.c. monitoring. [c]Neat (35%) aqueous tetrafluoroboric acid. [d]Identified by its ^{13}C-n.m.r. spectrum[2].

From these results, tetrafluoroboric acid is obviously, for various carbohydrate protection and deprotection reactions, an outstanding catalyst which considerably diminishes necessary operations and, as compared to *O*-detritylation by boron trifluoride-etherate[7] or *O*-desilylation by tetrabutylammonium fluoride[8], the cost.

For methyl 3-amino-3-deoxy-α-D-glucopyranoside[20] (used in this investigation), an efficient, stereospecific synthesis, starting from methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-allopyranoside[21] and taking advantage of a sulfonate–azide SN2 reaction, was used (total yield 73%). It is noteworthy that the displacement reaction in the presence of the 4,6-cyclic acetal led to an inseparable mixture of substitution and elimination products[22] (7:3, judged from the ^{1}H-n.m.r. spectrum), whereas, after *O*-debenzylidenation, the same reaction led to the substitution product only.

EXPERIMENTAL

General. — Melting points, determined with a Tottoli apparatus, are uncorrected; optical rotations were measured with a Perkin–Elmer 141 polarimeter; n.m.r. spectra were recorded with a Bruker WH-90 DS instrument. T.l.c. was performed on silica gel, Merck 5554; column chromatography[23] was accomplished on silica gel 60, 230–400 mesh (Merck 9385).

General procedure

Benzylidenation. — To a 5% solution of the educt (5 mmol) in *N,N*-dimethylformamide (Merck 3034) are added benzaldehyde dimethyl acetal[3] (0.8 mL, 5.35 mmol) and tetrafluoroboric acid (54% in ether, Merck–Schuchardt 800172; 0.68 mL, 5 mmol). After quantitative reaction, triethylamine (0.7 mL, 5 mmol) is added, and the solvent is evaporated. Then chloroform (40 mL) is added, the mixture filtered through a short column of silica gel (20 mL), and, together with the washings (150 mL of chloroform), evaporated to dryness. Isolation and purification are effected by the procedures given in the literature and in Table III, respectively.

*Acetal cleavage, O-detritylation and O-de(*tert*-butyldimethylsilyl)ation.* — To a 5% solution of the educt (5 mmol) in acetonitrile is added tetrafluoroboric acid (35% in water, Merck 171; 1.0 mL, 5 mmol). After quantitative reaction (t.l.c., 5 to 30 min at room temperature), triethylamine (0.7 mL, 5 mmol) is added, and the solvent is evaporated. Purification of the products is achieved as before.

Tetra-N-*(benzyloxycarbonyl)-4",6"-O-cyclohexylidenekanamycin A* (ref. 13, **16**). — This was prepared from **15** [m.p. 273° (dec.), $[\alpha]_D^{20}$ +77.5° (*c* 1.34, *N,N*-dimethylformamide); ref. 13, $[\alpha]_D^{20}$ +68° (*c* 2, *N,N*-dimethylformamide); 5.1 g, 5 mmol] according to the general procedure for the benzylidenation reaction, but using cyclohexanone dimethyl acetal[14] (1.44 g, 10 mmol). After quantitative reaction [2 h; t.l.c. (5:1 ethyl acetate–methanol) R_F 0.55 (**16**), 0.21 (**15**)], the mixture was poured into a boiling, saturated, aqueous solution of sodium hydrogen-

TABLE III

DATA FOR PRODUCTS OBTAINED BY APPLICATION OF THE GENERAL PROCEDURES[a]

Compound	*Isolation*	*m.p. (degrees)*	$[\alpha]_D^{20}$[b] *(degrees)*	R_f[c]	*Analysis*	*Calc.*	*Found*	^{1}*H-N.m.r. data*
8	residue digested with hot ethanol; **8** insoluble	210–212	+108.6 (1, A)	0.91 (A)	C H N	70.27 5.90 3.04	69.94 5.84 2.90	(dimethyl sulfoxide-d_6) 3.5–4.25 (m, 6 H, H-2,3,4,5,6,6'), 4.53 and 4.74 (AB, 2 H, O-CH_2-Ph, J 8.5 Hz), 5.00 (d, 1 H, H-1, $J_{1,2}$ 3 Hz), 5.25 (d, 1 H, OH, J 4 Hz), 5.69 (s, 1 H, -CH-Ph), 7.1–8.0 (m, 15 H, 3 Ph), and 8.50 (d, 1 H, NH, J 5 Hz)
10	crystallization from ethyl acetate–cyclohexane	217–218 (dec.)	+62.5 (1, B)	0.83 (B)	C H N	59.83 7.14 3.67	59.54 7.08 3.54	(chloroform-d) 1.42 (s, 9 H, CMe_3), 3.46 (s, 3 H, OCH_3), 5.49 (s, 1 H, -CH-Ph), and 7.25–7.55 (m, 5 H, Ph)
12	crystallization from ethyl acetate–cyclohexane	234–236 (dec.)	−56.2 (1, B)	0.79 (B)	C H N	59.83 7.14 3.67	59.68 7.20 3.57	(dimethyl sulfoxide-d_6) 1.39 (s, 9 H, CMe_3), 3.42 (s, 3 H, OCH_3), 5.53 (s, 1 H, -CH-Ph), and 7.39 (s, 5 H, Ph)
14	chromatography (1:3 chloroform–petroleum ether)	syrup (ref. 12, 64–65)	+20.4 (2.1, C)	0.85 (C)				(chloroform-d) 1.32 and 1.47 (6 H, CMe_2), 4.66 (d, 1 H, H-2, $J_{1,2}$ 3.5 Hz), 5.98 (s, 1 H, Ph-CH), 6.05 (d, 1 H, H-1), and 7.1–7.7 (m, 20 H, 4 Ph)
22	chromatography (1.1 ethyl acetate–toluene)	amorphous	+61.5 (2.09, A)	0.21 (D)	C H	46.43 4.09	46.12 3.94	(chloroform-d) 3.12 (2 H, 2 HO), 3.39 (s, 3 H, OCH_3), 3.8–4.2 (m, 4 H, H-4,5,6,6'), 4.94 (d, 1 H, H-1, $J_{1,2}$ 3.5 Hz), 5.10 (t, 1 H, H-2, $J_{2,3}$ 3.5 Hz), 5.51 (broad s, 1 H, H-3), and 7.2–7.9 (m, 9 H, *Ph*CO, Br-C_6H_4-SO_2)
24	chromatography (1:1 ethyl acetate–toluene)	syrup	+62.2 (6.6, C)	0.58 (D)				(chloroform-d) 2.38 (1 H, HO), 3.46 (s, 3 H, OCH_3), 3.5–4.1 (m, 4 H, H-5,6,6', and OH), 4.46 (d, 1 H, H-4, $J_{4,5}$ 6.5 Hz), 5.35 (d, 1 H, H-1, $J_{1,2}$ 3 Hz), 5.67 (d, 1 H, H-2), and 7.3–8.2 (m, 5 H, PhCO)
26	chromatography (1.1 ethyl acetate–toluene)	syrup	+50.1 (5.36, C)	0.50 (D)				($CDCl_3$–D_2O) 2.46 (s, 6 H, 2 CH_3-Ph), 3.28 (s, 3 H, OCH_3), 3.6–4.0 (m, 4 H, H-4,5,6,6'), 4.31 (dd, 1 H, H-2, $J_{1,2}$ 3, $J_{2,3}$ 7 Hz), 4.77 (d, 1 H, H-1), 4.88 (dd, 1 H, H-3), and 7.1–7.9 (m, 8 H, 2 CH_3-C_6H_4-SO_2)
28	ethyl acetate–cyclohexane	amorphous	+79.5 (2.28, B)	0.14 (D)	C H N	65.17 5.33 3.90	64.88 5.40 3.74	[d]

[a] Compounds already known in the literature, and according in their data with those reported, are omitted. [b] Concentration (c) and solvent given in parentheses (A, pyridine, B, *N*,*N*-dimethylformamide, C, chloroform). [c] Eluant A, 3:1 ethyl acetate–methanol, B, 9:1 ethyl acetate–methanol, C, 1:2 ethyl acetate–toluene, and D, 1:1 ethyl acetate–toluene. [d] Not significant.

carbonate (150 mL), and the precipitate collected by filtration and washed with water (60 mL); yield, 5.05 g (91.7%); m.p. 283–284°, $[\alpha]_D^{20}$ +68.8° (*c* 1, *N,N*-dimethylformamide); ref. 13, $[\alpha]_D^{20}$ +60° (*c* 1, *N,N*-dimethylformamide).

1,2-O-Isopropylidene-α-D-glucofuranurono-6,3-lactone[15] (**18**). — A mixture of powdered **17** (Fluka 49340; 1.76 g, 10 mmol), acetone (Merck 14; 25 mL), and ethereal tetrafluoroboric acid (1.5 mL, 12 mmol) was stirred at room temperature until reaction was complete [10–20 min; t.l.c. in 1:2 toluene–ethyl acetate, R_F 0.67 (**18**), 0.0 (**17**)]. After neutralization with anhydrous sodium carbonate, filtration, and evaporation, **18** crystallized from chloroform–cyclohexane; yield 1.92 g (89.1%).

1,2:5,6-Di-O-isopropylidene-α-D-glucofuranose[5] (**20**). — This was obtained by the reaction of D-glucose (Merck 8337; 3.6 g, 20 mmol) with acetone (50 mL) in the presence of molecular sieve (Union Carbide, type 4A, powder; 0.4 g) and ethereal tetrafluoroboric acid (2.7 mL, 20 mmol) for 30 min at 50° [t.l.c. (ethyl acetate) R_F 0.66]. After addition of triethylamine (2.8 mL, 20 mmol) and filtration, the solvent was evaporated. The residue was digested with warm chloroform (100 mL), and the digest washed with water (30 mL), dried (sodium sulfate), and evaporated to a syrup. From its solution in hot cyclohexane, **20** crystallized; yield, 4.44 g (85.4%).

1,2-O-Isopropylidene-α-D-glucofuranose[5] (**35**). — To a solution of **20** (2.6 g, 10 mmol) in 1:1 acetone–water (50 mL) was added tetrafluoroboric acid (35% in water; 2.0 mL, 10 mmol) in 0.2 mL portions during 5 h; t.l.c. monitoring (ethyl acetate) beside **35** (R_F 0.26) then showed traces of **20** and very little D-glucose. After addition of triethylamine (1.4 mL, 10 mmol), the solvent was evaporated, and from the residue, after dissolution in ethanol (30 mL), filtration through silica gel (10 mL), and addition of petroleum ether (b.p. 60–80°), **35** was obtained; yield 2.1 g (96.4%).

*Methyl 3-(*tert*-butoxycarbonyl)amino-3-deoxy-α-D-glucopyranoside* (**9**). — This was prepared from methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-allopyranoside[21] by the sequence of simple reactions described generally in the following.

(1) Treatment with 4-bromobenzenesulfonyl chloride (2 equiv.) in a 10% pyridine solution for 24 h at 70°, yielding methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-brosyl-α-D-allopyranoside (**21**); 95%; m.p. 213–215° (from ethanol), $[\alpha]_D^{20}$ +59.8° (*c* 1, chloroform); ^{1}H-n.m.r. (chloroform-*d*): δ 3.43 (s, 3 H, OCH_3), 3.65–4.45 (m, 4 H, H-4,5,6,6'), 5.00 (d, 1 H, H-1, $J_{1,2}$ 3.5 Hz), 5.17 (t, 1 H, H-2, $J_{2,3}$ 3.5 Hz), 5.48 (m, 2 H, H-3 and Ph-C*H*), 7.14–7.75 (m, 12 H, *Ph*-CH, Br-C_6H_4-SO_2, *m*- and *p*-*H* of Ph-CO), and 8.07–8.20 (m, 2 H, *o*-*H* of Ph-CO).

Anal. Calc. for $C_{27}H_{25}BrSO_9$ (605.4): C, 53.56; H, 4.16. Found: C, 53.40; H, 4.07.

(2) *O*-Debenzylidenation according to the general procedure, to afford methyl 2-*O*-benzoyl-3-*O*-brosyl-α-D-allopyranoside (**22**; see Table III).

(3) Nucleophilic substitution by sodium azide (3 equiv.) in 10% *N,N*-dimethylformamide solution for 2 h at 130°, with formation of methyl 3-azido-2-*O*-

benzoyl-3-deoxy-α-D-glucopyranoside; 90%; m.p. 106–108° (from ethyl ether–cyclohexane), $[\alpha]_D^{20}$ +225.5° (*c* 1.45, pyridine); ^{1}H-n.m.r. (dimethyl sulfoxide-d_6): δ 3.32 (s, 3 H, OCH_3), 3.35–4.1 (m, 5 H, H-3,4,5,6,6′), 4.70 (s, 1 H, OH), 4.80 (dd, 1 H, H-2, $J_{1,2}$ 3.5, $J_{2,3}$ 8 Hz), 4.96 (d, 1 H, H-1), 5.86 (d, 1 H, OH, *J* 4.5 Hz), and 7.45–8.1 (m, 5 H, Ph-CO).

Anal. Calc. for $C_{14}H_{17}N_3O_6$ (323.3): C, 52.01; H, 5.30; N, 13.00. Found: C, 52.56; H, 5.52; N, 12.99.

(4) Zemplén *O*-debenzoylation, leading to methyl 3-azido-3-deoxy-α-D-glucopyranoside; 98%; m.p. 123–125° (from ethyl acetate–cyclohexane), $[\alpha]_D^{20}$ +176.6° (*c* 1.87, pyridine); ^{1}H-n.m.r. (dimethyl sulfoxide-d_6): δ 3.0–3.7 (m, 6 H, H-2,3,4,5,6,6′), 3.20 (s, 3 H, OCH_3), 4.34 (m, 2 H, H-1 and OH, $J_{1,2}$ 3 Hz), 5.21 and 5.28 (d each, 1 H each 2 OH, *J* 4.5 and 5.5 Hz, resp.).

Anal. Calc. for $C_7H_{13}N_3O_5$ (219.2): C, 38.36; H, 5.98; N, 19.16. Found: C, 38.26; H, 5.92; N, 18.74.

(5) Hydrogenation in the presence of Raney nickel in ethanol at 0.4 MPa, to give methyl 3-amino-3-deoxy-α-D-glucopyranoside[20] (95%).

(6) Reaction with *tert*-butyl dicarbonate (1.3 equiv.) in dimethyl sulfoxide (10% solution) for 2 h[11] at 60°, leading to **9** (92%); m.p. 170–171° (from ethyl acetate), $[\alpha]_D^{20}$ +136.5° (*c* 1, *N*,*N*-dimethylformamide); ^{1}H-n.m.r. (dimethyl sulfoxide-d_6): δ 1.40 (s, 9 H, CMe_3), 3.0–3.7 (m, 6 H, H-2,3,4,5,6,6′), 3.28 (s, 3 H, OCH_3), 4.4–4.6 (m, 3 H, H-1 and 2 OH), 4.74 (d, 1 H, OH, *J* 4 Hz), and 6.53 (d, 1 H, NH, *J* 5 Hz).

Anal. Calc. for $C_{12}H_{23}NO_7$ (293.3): C, 49.14; H, 7.90; N, 4.78. Found: C, 48.71; H, 7.93; N, 4.68.

Reaction of **21** with azide gave an inseparable mixture of products from which, after *O*-debenzoylation, methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranoside [m.p. 158–160° (chloroform–petroleum ether), $[\alpha]_D^{20}$ +219.6° (*c* 0.95, chloroform); ^{1}H-n.m.r. (chloroform-*d*): δ 2.32 (broad s, 1 H, OH), 3.48 (s, H, OCH_3), 3.5–4.0 (m, 5 H, H-3,4,5,6,6′), 4.29 (dd, 1 H, H-2, $J_{1,2}$ 3, $J_{2,3}$ 8 Hz), 4.77 (d, 1 H, H-1), 5.55 (s, 1 H, Ph-C*H*), and 7.2–7.7 (m, 5 H, *Ph*-CH); *Anal.* Calc. for $C_{14}H_{17}N_3O_5$ (307.3): C, 54.72; H, 5.77; N, 13.68. Found: C, 54.79; H, 5.63; N, 12.78] was isolated in 62% yield; hydrogenation in the presence of Raney nickel gave methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranoside[24] (95%).

1,2-O-Isopropylidene-6-O-trityl-α-D-glucofuranose[12] (**13**). — A solution of 1,2-*O*-isopropylidene-α-D-glucofuranose[5] (**35**; 2.2 g, 10 mmol) and chlorotriphenylmethane (3.15 g, 12 mmol) in pyridine (15 mL) was kept at room temperature. After quantitative reaction [8 h, t.l.c. (ethyl acetate) R_F 0.26 (**35**) and 0.86 (**13**)], the mixture was poured into water (100 mL) under vigorous stirring. From the precipitate (4.63 g) **13** was isolated by chromatography (2:1 ethyl acetate–toluene), and recrystallized from diisopropyl ether; yield 4.05 g (87.6%); m.p. 141–143° (ref. 12: amorphous), $[\alpha]_D^{20}$ −5.0° (*c* 1, chloroform); ^{1}H-n.m.r. (chloroform-*d*): δ 1.29 and 1.45 (2 s, 3 H each, CMe_2), 2.86 (d, 1 H, OH, *J* 2 Hz), 3.2–3.6 (m, 3 H, H-6,6′

and OH), 4.0–4.35 (m, 3 H, H-3,4,5), 4.50 (d, 1 H, H-2, $J_{1,2}$ 3.5 Hz), 5.95 (d, 1 H, H-1), and 7.1–7.6 (m, 15 H, CPh_3).

Anal. Calc. for $C_{28}H_{30}O_6$ (462.5): C, 72.71; H, 6.54. Found: C, 72.95; H, 6.79.

*Methyl 6-(benzyloxycarbonyl)amino-6-deoxy-α-*D*-glucopyranoside* (**34**). — To a solution of methyl 6-amino-6-deoxy-α-D-glucopyranoside[25] (11.6 g, 60 mmol) and sodium carbonate (6.4 g, 60 mmol) in 1:1 water–acetone (120 mL) was added benzyl chloroformate (90–95%; 8.5 mL, 65 mmol) under vigorous stirring at room temperature. After 30 min, acetone (120 mL) was added, the precipitate formed filtered off, and the filtrate evaporated *in vacuo*. Then chloroform (100 mL) was added; after drying (sodium sulfate), the volume was lessened to 50 mL by evaporation, and **35** was precipitated by addition of hot cyclohexane (~100 mL). Recrystallization was effected from ethyl acetate; yield 17.3 g (88.4%); m.p. 114–115°, $[\alpha]_D^{20}$ +101.9° (*c* 1.32, *N,N*-dimethylformamide); ^{1}H-n.m.r. (dimethyl sulfoxide-d_6): δ 2.8–3.6 (m, 6 H, H-2,3,4,5,6,6'), 3.18 (s, 3 H, OCH_3), 4.50 (d, 1 H, H-1, $J_{1,2}$ 3.5 Hz), 4.7–4.9 (m, 2 H, 2 OH), 7.18 (d, 1 H, NH, *J* 5 Hz), and 7.32 (s, 5 H, CH_2-*Ph*).

Anal. Calc. for $C_{15}H_{21}NO_7$ (327.3): C, 55.04; H, 6.47; N, 4.28. Found: C, 54.91; H, 6.54; N, 4.15.

*Methyl 6-(benzyloxycarbonyl)amino-2-*O*-(*tert*-butyldimethylsilyl)-6-deoxy-α-*D*-glucopyranoside* (**33**). — To **34** (3.27 g, 10 mmol) and imidazole (0.75 g, 11 mmol) in *N,N*-dimethylformamide (50 mL) was added *tert*-butylchlorodimethylsilane (1.57 g, 10.5 mmol) at room temperature. After the starting material had disappeared [t.l.c., ethyl acetate, R_F 0.73 (**33**), 0.1 (**34**)], methanol (1 mL) was added, the solvent evaporated, and **33** isolated from the residue by chromatography (1:1 ethyl acetate–toluene); yield 2.72 g (61.6%); m.p. 98–99°, $[\alpha]_D^{20}$ +67.8° (*c* 1.41, *N,N*-dimethylformamide); ^{1}H-n.m.r. (chloroform-*d*): δ 0.11 (s, 6 H, $SiMe_2$), 0.91 (s, 9 H, $SiCMe_3$), 2.56 (broad s, 1 H, OH), 3.2–3.9 (m, 7 H, H-2,3,4,5,6,6' and OH), 3.35 (s, 3 H, OCH_3), 4.56 (d, 1 H, H-1, $J_{1,2}$ 3.5 Hz), 5.14 (broad s, 3 H, CH_2-Ph and NH), and 7.35 (s, 5 H, CH_2-*Ph*).

Anal. Calc. for $C_{21}H_{35}NO_7Si$ (441.6): C, 57.12; H, 7.99; N, 3.17. Found: C, 56.99; H, 7.84; N, 3.03.

*2',3',4',2''-Tetra-*O*-benzoyltetra-*N*-(benzyloxycarbonyl)-4'',6''-*O*-cyclohexylidenekanamycin A* (ref. 13, **27**) was prepared from **16** (4.4 g, 4 mmol) by treatment with benzoyl chloride (2.8 mL, 24 mmol) in pyridine (40 mL) overnight at room temperature.

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