# Reactions of Relevance to the Chemistry of Aminoglycoside Antibiotics. Part 15.† The Selective Modification of Neamine by Radical-induced Deamination

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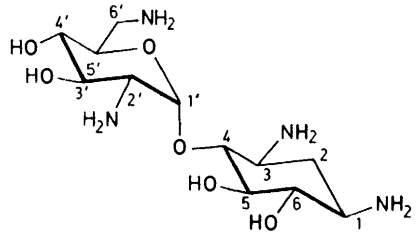
The reaction of neamine tetraformamide tetra-acetate with phosphorus oxychloride and triethylamine has been studied. Isocyanide formation was found to proceed in stepwise fashion. The radical-induced reduction of the resultant derivatives by tri-n-butylstannane leads to the corresponding deaminated aminoglycoside derivatives. In this way five new derivatives of neamine have been prepared for (eventual) biological evaluation.

THE aminoglycoside antibiotics occupy a central role as valuable chemotherapeutic agents for the treatment of serious gram negative infections. They are, however, potentially toxic to varying degrees, and may also be inactivated by resistant strains of bacteria. Thus, there is a strong incentive for the preparation of new structural variants which may lead to a better understanding of structure–activity relationships, and hence to antibiotics which have improved pharmacological properties.[1]

Since the number and relative positions of the various amino-groups in these antibiotics is of crucial importance, it is of interest to examine the effect engendered by the selective replacement of a primary amino-function by a hydrogen atom. Although this transformation can be accomplished on simple substrates by ionic reactions,[2,3] these are incompatible with the carbohydrate framework. However, we have recently extended the utility of the radical-induced deamination of isocyanides by tri-n-butylstannane, and shown that it is a general reaction of considerable value for the modification of natural products.[4,5]



(1)

The pseudodisaccharide neamine (1), isolated from *Streptomyces* cultures or from hydrolysis of neomycins and other antibiotics, has four secondary hydroxy-groups and four primary amine groupings. It was selected as a suitable model for preliminary studies. Performylation with *p*-nitrophenyl formate followed by peracetylation with acetic anhydride in pyridine afforded the desired tetra-acetate tetraformamide (2) in essentially quantitative yield. The tetraformamide has been mentioned before,[6] but not characterised. Phosphorus oxychloride and triethylamine in dichloromethane as solvent proved to be a very efficient combination for the dehydration of the formamide moiety to the isocyanide grouping. From the experimental viewpoint, examination of Table 1 reveals that control of reaction temperature and time is essential in these reactions. Moreover, the excess of phosphorus oxychloride must be quenched with gaseous ammonia at low temperature in order to minimise over-reaction during work-up. In this way, it was possible to capitalise on the small differences in activation energy for isocyanide formation at the four sites, and hence to isolate all three of the intermediates between the mono- (3) and the tetra-isocyanide (6) (Scheme 1).

TABLE 1

Reaction of the tetraformamide (2) with phosphorus oxychloride and triethylamine in dichloromethane

| | | Isolated yields (%) | | | | |
|---|---|---|---|---|---|---|
| $T$/°C | $t$/h | (2) | (3) | (4) | (5) | (6) |
| −38 | 8 | <10 | 41 | 21 | | |
| −18 | 27 | | 19 | 39 | 12 | |
| 0 | 26 | | | 29 | 38 | 6 |
| 8 | 24 | | | | | 59 |

The observed order for the essentially stepwise formation of isocyanides deserves some comment, particularly since the least hindered formamide at C-6′ is not the first to yield an isocyanide. It seems reasonable to postulate that steric acceleration in the rate-determining breakdown of the intermediate (7) contributes to the enhanced reactivity at C-1 over C-6′, while formation of this intermediate is rate determining for the even more hindered formamides at C-3 and C-2′.

With the obtention of the four isocyano-neamine derivatives, we then focused our attention on the tri-n-butylstannane reduction. Model studies on the deamination of n-octadecyl isocyanide had shown that formation of the primary carbon radical required reflux for 7 h in xylene with more than one equivalent of radical initiator.[4] In the event however, all isocyano-neamine derivatives were completely deaminated within 2 h in refluxing benzene (Scheme 1). Nevertheless, it was possible to demonstrate the selective removal of the secondary iso-

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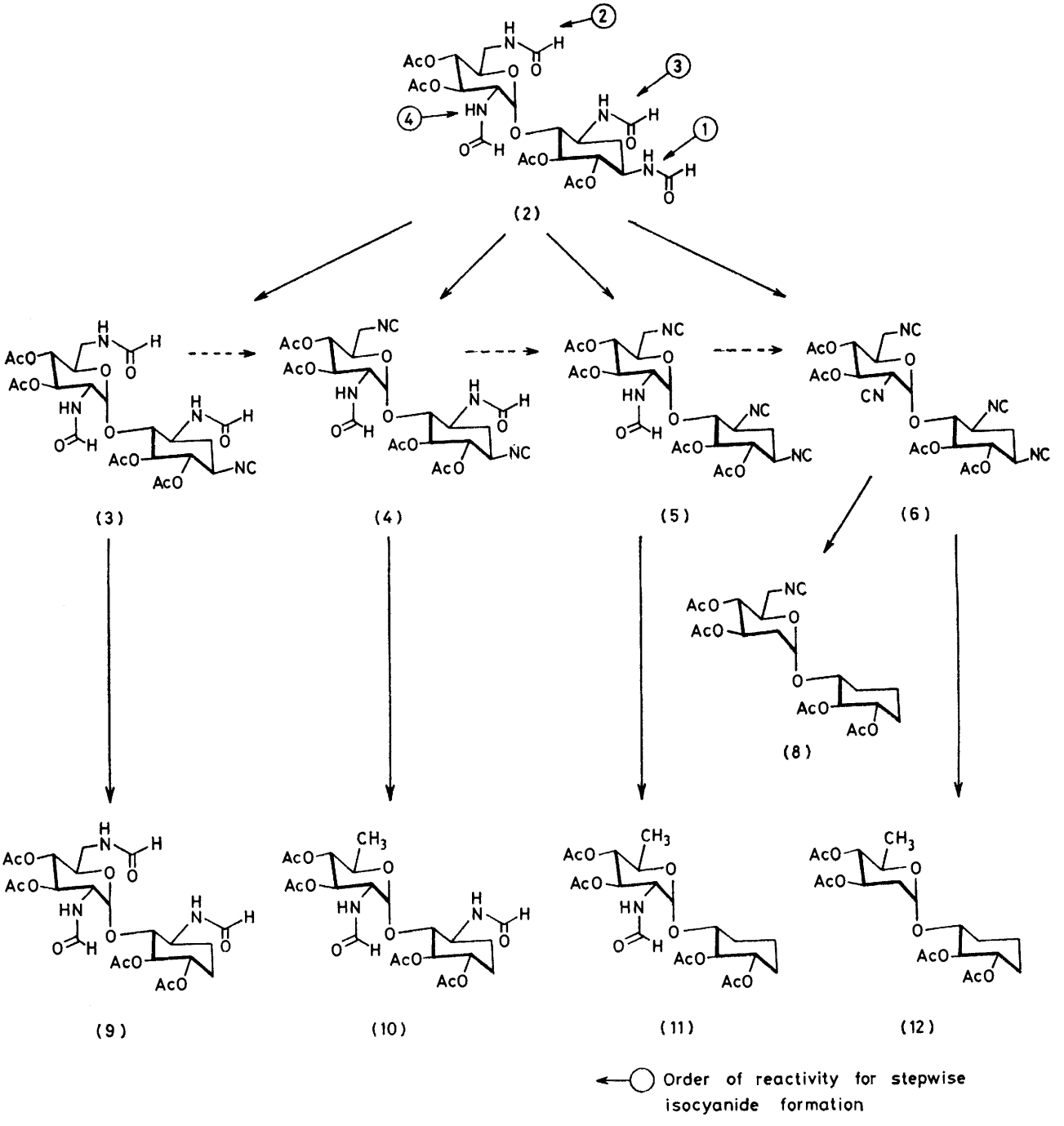
cyanide groupings in the tetraisocyanide (6) by running the reaction in benzene solution at 70—72 °C, and hence to isolate the partially deaminated isocyanide (8).

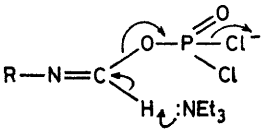
It is appropriate at this point to indicate that the position 3. Mass spectroscopy with chemical ionisation was particularly helpful in elucidating the stepwise pathway for formation of isocyanides. Neamine derivatives tend to fragment into the corresponding sugar and




SCHEME 1

structural assignments for compounds (2)—(11) are based primarily on consideration of the n.m.r. and mass spectra. In addition we have made the assumption that the amine at position 1 is less hindered than that at cyclitol moieties as shown for compound (12) (Scheme 2). The n.m.r. spectra of neamine derivatives containing several formamide groupings proved to be difficult to interpret because of multiple rotamerism. For this

reason, the deaminated triformamide (9) was converted into the isocyanide derivative (13) in order to facilitate structural assignments.



(7)

R = sugar

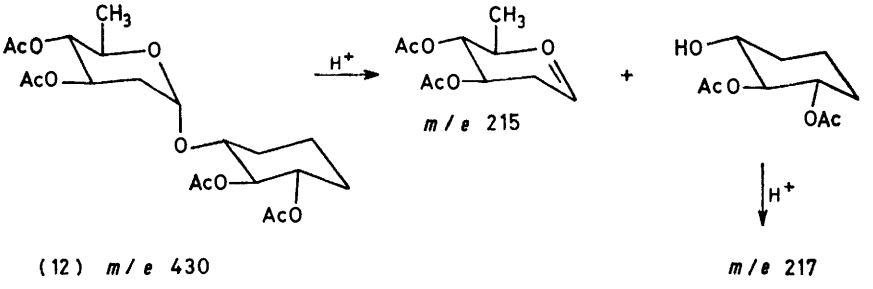
Comparison of the proton chemical shifts for the tetra- (6) and the tri-isocyanide (13) (Table 2) show that the

TABLE 2

$^1$H N.m.r. data for compounds (6) and (13)

| | Chemical shift (δ) | |
|---|---|---|
| Proton | (6) | (13) |
| H-1 | 3.80 | |
| H-3 | 3.77 | 3.68 |
| H-4 | 4.10 | 3.97 |
| H-5 } | 5.05 } | 5.08 } |
| H-4′ } | 5.04 } | 5.05 } |
| H-6 | 5.12 | 4.82 |
| H-1′ | 5.42 | 5.45 |
| H-2′ | 3.95 | 3.94 |
| H-3′ | 5.49 | 5.50 |
| H-5′ | 4.50 | 4.55 |
| H-6′ | 3.75 3.51 | 3.75 3.51 |

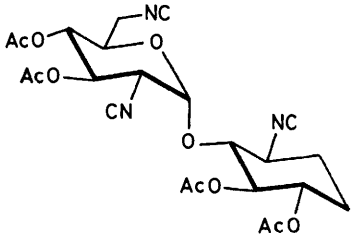
peak at δ 3.80 indicating substitution at C-1 has disappeared. Moreover, the triplet for H-6 in (6) becomes a triplet of doublets in (13). The chemical shift and



(12) *m/e* 430 *m/e* 217

SCHEME 2

splitting pattern of H-4 remains unchanged in the two compounds. The structure of the tri-isocyanide (13) is



(13)

also supported by its $^{13}$C n.m.r. spectrum (Table 3). The downfield chemical shift of C-4 relative to neamine [7,8] can be explained by acetylation at C-5 and the presence of an isocyanide group at C-3.[9] The chemical shift of the C-6 nucleus (66.6 p.p.m.) is attributable to the lack of a β effect, thus implying the presence of a methylene group at C-1. Proton chemical shifts for other deaminated products are listed (Table 4).

The results described herein have been achieved in a direct manner by using the selectivity inherent in the

TABLE 3

$^{13}$C N.m.r. data for the tri-isocyanide (13)*

| C | Chemical shift (δ) | C | Chemical shift (δ) |
|---|---|---|---|
| 1 | 25.2 [a] | 1′ | 96.1 |
| 2 | 27.4 [a] | 2′ | 54.1 [b] |
| 3 | 54.5 [b] | 3′ | 68.4 |
| 4 | 79.4 | 4′ | 70.6 |
| 5 | 73.8 | 5′ | 67.3 [c] |
| 6 | 66.6 [c] | 6′ | 41.2 |

[a,b,c] Assignments may be interchanged.

* δ Values recorded as p.p.m. relative to internal tetramethylsilane; run in $CDCl_3$ at 15.08 MHz using a 2 mm microprobe.

neamine molecule itself. In addition, we have also shown that the readily prepared isothiocyanates of primary amines are excellent candidates for radical deamination.[4] In principle, an even larger variety of selectively deaminated products can be prepared, by a judicious sequence of selective protection.[10] This technique for the direct deamination of aminoglycoside antibiotics thus offers a complementary method to the alternatives of total sythesis [11] or mutasynthesis.[12] In addition it is certainly more economic.

## EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were recorded on a Perkin-Elmer 257 spectrometer and $^1$H n.m.r. spectra were measured in deuteriochloroform solution with tetramethylsilane as internal standard unless otherwise stated. Mass spectra were recorded with an A.E.I. MS9 instrument. Optical rotations were measured on a Perkin-Elmer 141 polarimeter. All solvents and reagents were purified and dried by standard techniques.

5,6,3′,4′-*Tetra*-O-*acetyl*-1,3,2′,6′-*tetra*-N-*formylneamine*(2). —A mixture of neamine (6.3 g) and *p*-nitrophenyl formate (18.4 g) in aqueous dimethylformamide (80 ml; 50%) was stirred at room temperature for 36 h. After evaporation of the solvent, ether was added slowly and the mixture was stirred for 2 h. Filtration gave the crude tetraformamide which was passed through a column of Amberlite resin (150

ml) in aqueous solution. After evaporation of the eluant the dry tetraformamide was suspended in acetic anhydride (135 ml) and pyridine (240 ml) and stirred at room temperature for 2 days until a clear solution was formed. Removal of the excess of solvent and reagent *in vacuo* followed by azeotropic distillation *in vacuo* with dry toluene yielded a colourless powder. This was reprecipitated by slow addition of heptane to a chloroform solution to give the desired compound as a non-crystalline powder (11.31 g, 96%). This was generally used without further purification. Chromatography on silica gel (tetrahydrofuran–benzene; 7 : 1) of a small sample gave a white amorphous powder, m.p. 170—175 °C, $[\alpha]_D^{20}$ +81.7 (*c*, 13 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 3 425 (NH), 1 749 (ester), and 1 691 (amide) $cm^{-1}$.

TABLE 4

$^1H$ N.m.r. data for deaminated products (8) and (10)—(12)

| | Chemical shift (δ) | | | |
|---|---|---|---|---|
| Proton | (8) | (10) | (11) | (12) |
| H-1 | | | | |
| H-3 | | 4.00 | | |
| H-4 | 3.63 | 3.64 | 3.64 | 3.55 |
| H-5 | 4.97 | 5.06 | 5.00 | 4.95 |
| H-4′ | 4.80 | 4.82 | 4.81 | 4.69 |
| H-6 | 4.77 | 4.75 | 4.76 | 4.75 |
| H-1′ | 5.07 | 4.87 | 4.87 | 4.95 |
| H-2′ | | 4.42 | 4.35 | |
| H-3′ | 5.25 | 5.13 | 5.13 | 5.20 |
| H-5′ | 4.05 | 3.98 | 3.91 | 3.92 |
| H-6′ | 3.5 | 1.17 | 1.17 | 1.14 |
| | | (Me) | (Me) | (Me) |

5,6,3′,4′-*Tetra*-O-*acetyl*-1,3,2′,6′-*tetradeamino*-1,3,2′,6′-*tetraisocyanoneamine* (6).—To a stirred solution of the tetra-acetate tetraformamide (2) (602 mg, 1 mmol) in dichloromethane (70 ml) with cooling at −40 °C was added triethylamine (2 g) and phosphorus oxychloride (0.74 ml). The mixture was allowed to warm to 8 °C and maintained at this temperature for 25 h. After cooling to 0 °C, phosphorus oxychloride was hydrolysed by the addition of an ice cold aqueous solution of sodium hydrogencarbonate. The organic layer was separated and the aqueous phase thoroughly extracted with chloroform. The combined extracts were dried ($Na_2SO_4$) and the solvent was removed to give a brown residue which was purified by column chromatography on silica gel, eluting successively with chloroform–methanol (9 : 1) and then on a second column with benzene–tetrahydrofuran (4 : 1). The resultant colourless oil was purified by repeated crystallisation from diethyl ether to yield the required *tetraisocyanide* (6) (314 mg, 59%), m.p. 223—224 °C, $[\alpha]_D^{20}$ +83.4° (*c*, 1.2 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 2 153 (NC) and 1 767 (ester) $cm^{-1}$, *m/e* 587, 531 ($M^+ + C_4H_9$, $M + H^+$), 471 ($MH^+$ — HOAc) (chemical ionisation, isobutane), 513 ($M^+ + 1$), 446 (531 — HOAc), 265 (sugar), 245 (cyclitol), 205 (265 — HOAc), 177 (265 — CO), and 145 (205 — HOAc) (Found: C, 53.95; H, 5.05; N, 10.45. $C_{24}H_{26}N_4O_{10}$ requires C, 54.34; H, 4.94; N, 10.56%).

*Tri-n-butyltin Hydride Reduction of the Tetraisocyanide* (6).—A solution of the tetraisocyanide (6) (170 mg, 0.32 mmol) and azobisisobutyronitrile (AIBN) (16 mg) in dry benzene (75 ml) was added dropwise to a refluxing solution of tri-n-butylstannane (900 mg) in benzene (25 ml) under nitrogen. Heating was contained for 2 h. Removal of solvent and column chromatography on silica gel (tetrahydrofuran–benzene; 3 : 22) gave the fully deaminated product as a crystalline powder (112 mg, 81%). Further recrystallisation gave the *tetra-acetate* (12) as long needles (99 mg, 72%), m.p. 180 °C (from ether–hexane), $[\alpha]_D^{20}$ +62.9° (*c*, 1.2 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 1 745 $cm^{-1}$, δ 1.14 (3 H, d, *J* 6.5 Hz, $CH_3$), 3.55 (1 H, td, *J* 10.5 and 5.51 Hz, H-4), 4.75 (1 H, td, *J* 10.7 and 6 Hz, H-6), 4.95 (1 H, br, H-1′), and 5.20 (1 H, td, *J* 10.7 and 5.3 Hz, H-3), *m/e* 448 ($M + NH_4^+$), 234 (cyclitol — H + $NH_3$), 217 (cyclitol — $H^+$), 215 (sugar$^+$), 155 (215 — HOAc) (chemical ionisation, 140 °C, $NH_3$) (Found: C, 56.0; H, 7.0. $C_{20}H_{30}O_{10}$ requires C, 55.81; H, 7.03%).

*Tri-n-Butyltin Hydride Reduction of the Tetraisocyanide* (6). *Obtention of the Monoisocyanide* (8).—A mixture of the tetraisocyanide (6) (189 mg, 0.356 mmol) and AIBN (16 mg) in dry benzene (75 ml) was added to a solution of tri-n-butylstannane (830 mg) in dry benzene (25 ml) under nitrogen in an oil-bath maintained at 70—72 °C. The reaction was carefully monitored by t.l.c. and allowed to cool to room temperature after 2.5 h. Evaporation of solvent, column chromatography on silica gel (tetrahydrofuran–benzene; 3 : 2), and recrystallisation from ether gave the *monoisocyanide* (8) as white needles (102 mg, 63%), m.p. 170—171 °C, $[\alpha]_D^{20}$ +55.3° (*c*, 0.8 in $CHCl_3$), $\nu_{max.}$ 2 160 (NC) and 1 741 (ester) $cm^{-1}$, δ 3.5 (2 H, m, $CH_2NC$), and 5.25 and 4.95 (1 H, td, *J* 10.6 and 6 Hz; 1 H, br, $J \simeq 3$ Hz; H-3′ and H-1′), *m/e* 562, 556 ($M^+ + C_4H_9$, $M^+ + H$), 396 ($MH^+$ — HOAc), 240 (sugar), 217 (cyclitol — $H^+$), and 199 (217 — $H_2O$) (chemical ionisation, isobutane, 150 °C) (Found: C, 55.3; H, 6.45; N, 3.25. $C_{21}H_{29}NO_{10}$ requires C, 55.38; H, 6.42; N, 3.08%).

5,6,3′,4′-*Tetra*-O-*acetyl*-1,3,2′,6′-*tetradeamino*-2′-*formamido*-1,3,6′-*tri-isocyanoneamine* (5).—Triethylamine (2.5 ml) and phosphorus oxychloride (0.37 ml) were added to a stirred solution of the tetraformamide (2) (301 mg; 0.5 mmol) in dichloromethane (35 ml) with cooling at −40 °C. The mixture was kept at −78 °C for 3 h, and then at 0 °C for 26 h. After cooling to −78 °C, a gentle stream of dry ammonia was passed into the solution which was meanwhile allowed to warm to −10 °C. The resultant precipitate was filtered off and washed several times with chloroform. The combined organic extract was then evaporated, and the residue was filtered through a short silica gel column (tetrahydrofuran) and finally purified by column chromatography ($SiO_2$; benzene–tetrahydrofuran, 2 : 1) to yield the di-isocyanide (4) (82 mg, 29%), the tetraisocyanide (6) (16 mg, 6%), and the desired tri-isocyanide (5) (104 mg, 38%) as an amorphous powder, ' m.p.' 140—150 °C, $[\alpha]_D^{20}$ +48.0° (*c*, 1 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 3 418 (NH) 2 148 (NC), 1 758 (ester), and 1 691 (amide) $cm^{-1}$.

*Tri-n-butyltin Hydride Reduction of the Tri-isocyanide* (5).—A solution of the tri-isocyanide (5) (91.5 mg), AIBN (8 mg), and tri-n-butylstannane (500 mg) in dry benzene (100 ml) was heated under reflux for 2 h, cooled, and the solvent removed *in vacuo*. Column chromatography ($SiO_2$; benzene–tetrahydrofuran, 2 : 1) yielded a colourless oil from which the desired *monoformamide* (11) was obtained in crystalline form by slow evaporation of a solution in ether–hexane (36 mg, 45%), m.p. 182 °C, $[\alpha]_D^{20}$ + 39.5° (*c*, 0.4 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 3 420 (NH), 1 746 (ester) $cm^{-1}$, δ 1.17 (3 H, d, *J* 8 Hz, $CH_3$), 4.35 (1 H, td, 10.5 and 3.3 Hz, H-2′), 5.35 (1 H, d, *J* 10.5 Hz, NH), and 8.07 (s, 1 H, CHO); *m/e* 474 ($MH^+$), 258 (sugar$^+$), 217 (cyclitol — $H^+$) (chemical ionisation, isobutane, 180 °C) (Found: C, 53.0; H, 6.6; N, 3.15. $C_{21}H_{31}NO_{11}$ requires C, 53.27; H, 6.60; N, 2.96%).

5,6,3′,4′-*Tetra*-O-*acetyl*-1,3,2′,6′-*tetradeamino*-3,2′-*diformamino*-1,6′-*di-isocyanoneamine* (4).—Triethylamine (5 ml) and phosphorus oxychloride (0.74 ml) were added to a

solution of the tetraformamide (2) (602 mg, 1 mmol) in dichloromethane (70 ml) with cooling at −50 °C. The mixture was allowed to warm slowly to −18 °C and then maintained at this temperature for a further 27 h. It was then cooled to −78 °C, treated with gaseous ammonia, filtered and separated by column filtration as previously described. Column chromatography on silica gel (tetrahydrofuran–benzene, 1 : 1) yielded the tri-isocyanide (5) (66 mg, 12%) and the desired di-isocyanide (4) (222 mg, 39%). The monoisocyanide (3) (109 mg, 19%) was also eluted from the column with tetrahydrofuran. The di-isocyanide (4) precipitated from dichloromethane–hexane as an amorphous powder, ' m.p.' 165—170 °C, $[\alpha]_D^{20}$ +31.3° (*c*, 1 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 3 410 (NH), 1 741 (ester), 2 158 (NC), and 1 692 (amide) $cm^{-1}$.

*Tri-n-butyltin Hydride Reduction of the Di-isocyanide* (4).—A mixture of the di-isocyanide (4) (200 mg), AIBN (16 mg), and tri-n-butylstannane (1 g) in dry benzene (100 ml) was heated to reflux under nitrogen for 1 h. Solvent was removed and the crude residue was purified by column chromatography on silica gel. Elution with benzene–tetrahydrofuran (7 : 1) was continued until all tin residues had been eluted from the column. Further fractionation with tetrahydrofuran–benzene (1 : 1) gave the *diformamide* (10) as a colourless oil which crystallised slowly from ether at room temperature (104 mg, 57%), m.p. 212—214 °C, $[\alpha]_D$ +37.0: (*c*, 0.5 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 3 415 (NH), 1 749 (ester), and 1 692 (amide)$cm^{-1}$, δ 1.17 (3 H, d, *J* 7 Hz, $CH_3$), 3.64 (1 H, t, *J* 9.7 Hz, H-4), 4.00 (1 H, m, H-3), 4.42 (1 H, dt, *J* 10.7 and 4.3 Hz, H-2'), 5.6 (2 H, m, 2NH), and 8.06 and 8.18 (2 H, 2 s, 2 CHO), *m/e* 574 and 517 ($M + C_4H_9^+$, $M + H^+$), 258 (sugar), 260 (cyclitol − $H^+$) (chemical ionisation, isobutane, 180 °C) (Found: C, 51.35; H, 6.5; N, 5.5. $C_{22}H_{32}N_2O_{12}$ requires C, 51.16; H, 6.24; N, 5.42%).

*5,6,3',4'-Tetra-O-acetyl-1,3,2',6'-tetradeamino-3,2',6'-triformamido-1-isocyanoneamine* (3).— Triethylamine (5 ml) and phosphorus oxychloride (0.74 ml) were added to a stirred solution of the tetraformamide (2) (550 mg) in dry dichloromethane (70 ml) with cooling in a bath at −60 °C. The mixture was slowly allowed to warm to −38 °C and kept at this temperature for 8 h. After cooling to −78 °C, the excess of phosphorus oxychloride was quenched by gaseous ammonia as previously described for (4) and (5). Column chromatography on silica gel with tetrahydrofuran as eluant gave the di-isocyanide (4) (197 mg, 21%) and the desired monoisocyanide (3) (218 mg, 41%). Further elution of the column with methanol followed by crude separation ($SiO_2$; ethyl acetate–methanol, 3 : 1) gave less than 10% of starting material. The monoisocyanide (3) thus obtained was a colourless armorphous powder which was used without further purification, ' m.p.' 150—160 °C, $[\alpha]_D^{20}$ +74.7° (*c*, 1 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 3 421 (NH), 2 152 (NC), 1 755 (ester), and 1 690 (amide) $cm^{-1}$.

*Tri-n-butyltin Hydride Reduction of the Monoisocyanide* (3).—A mixture of the monoisocyanide (3) (190 mg), AIBN (20 mg), and tri-n-butylstannane (450 mg) in dry benzene (150 ml) was heated to reflux for 3 h, cooled, and poured directly on to a column ($SiO_2$; benzene–tetrahydrofuran, 7 : 1). Elution was continued to remove the tin residues. Final elution with benzene–tetrahydrofuran, 1 : 7 gave the *triformamide* (9) (111 mg, 61%) as a white amorphous powder, ' m.p.' 130—140 °C, $[\alpha]_D$ +82.6° (*c*, 0.7 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 3 411 (NH), 1 758 (ester), and 1 698 (amide) $cm^{-1}$ (Found: C, 48.9; H, 6.1; N, 7.65. $C_{23}H_{33}N_3O_{13}$ requires C, 49.37; H, 5.94; N, 7.51%).

*5,6,3',4'-Tetra-O-acetyl-1,3,2',6'-tetradeamino-3,2,6'-triisocyanoneamine* (13).—Triethylamine (1.25 ml) and phosphorus oxychloride (0.19 ml) were added to a stirred solution of the triformamide (9) (82 mg) in dichloromethane (20 ml) with cooling in a bath at −30 °C. The mixture was maintained at 8 °C for 10 h and then for a further 15 h at room temperature, and filtered directly through a silica gel column (tetrahydrofuran as eluant). Column chromatography on silica gel (tetrahydrofuran–benzene, 3 : 22) gave the *triisocyanide* (13) (56 mg, 76%) as a colourless oil, which crystallised from benzene by very slow addition of hexane as tiny square plates (42 mg, 57%), m.p. 113—115 °C (decomp.) (loss of benzene), $[\alpha]_D^{20}$ +105.6° (*c*, 0.7 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 2 151 (NC) and 1 760 (ester) $cm^{-1}$, *m/e* (200 °C) 506 ($M^+ + 1$), 446 (506 − HOAc), 265 (sugar), 224 (cyclitol), 205 (265 − HOAc), 177 (205 − CO), and 145 (205 − HOAc); δ 3.97 (1 H, t, *J* 9.5 Hz, H-4), 4.82 (1 H, ddd, *J* 10, 11, and 4.5 Hz, H-6), 3.75 (1 H, dd, *J* 16 and 3.3 Hz, H-6'$_1$), 3.51 (1 H, dd, *J* 16 and 3.1 Hz, H-6'$_2$) (Found: C, 59.65; H, 5.75; N, 7.25. $C_{23}H_{27}N_3O_{10}\cdot C_6H_6$ requires C, 59.69; H, 5.70; N, 7.20%).

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