

STEREOCONTROLLED ROUTES TO *cis*-HYDROXYAMINO SUGARS, PART VII: SYNTHESIS OF DAUNOSAMINE AND RISTOSAMINE*

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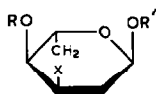
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ABSTRACT

The nitrogen of an allylic amine can serve as the fulcrum for stereocontrolled delivery of oxygen to an adjacent trigonal site, and *cis*-hydroxyamino sugars can thus be prepared. Methods for achieving the complementary procedure, namely, control of the delivery of nitrogen to an adjacent site by an allylic oxygen, are described. For example, treatment of methyl 2,3,6-trideoxy- α -L-erythro-hex-2-enopyranoside with trichloroacetonitrile gave an imidate ester which reacted with iodonium dicollidine perchlorate to give 2-trichloromethyl-(methyl 2,3,4,6-tetra-deoxy-2-iodo- α -L-altropyranosido)-[3,4-*d*]-2-oxazoline. Exhaustive reductive dehalogenation of this product followed by hydrolysis led to methyl *N*-acetyl- α -L-ristosaminide. An analogous series of reactions was used to prepare the corresponding daunosaminide.

INTRODUCTION

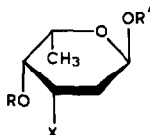
In 1980, we introduced a novel iodocyclization of allylic carbamates in which the allylic nitrogen acts as a fulcrum to guide the nucleophilic oxygen into a *cis*-vicinal relationship¹ (Scheme 1A). The utility of the procedure was first demonstrated by the synthesis of garosamine^{1,2} and the methodology has since been applied to the synthesis of holacosamine³, 4-*epi*-D-sibirosamine⁴, and naphthyridinomycin⁵.



1a X = NH₂, R = R' = H

1b X = NHAc, R = H, R' = Me

1c X = NHAc, R = Ac, R' = Me



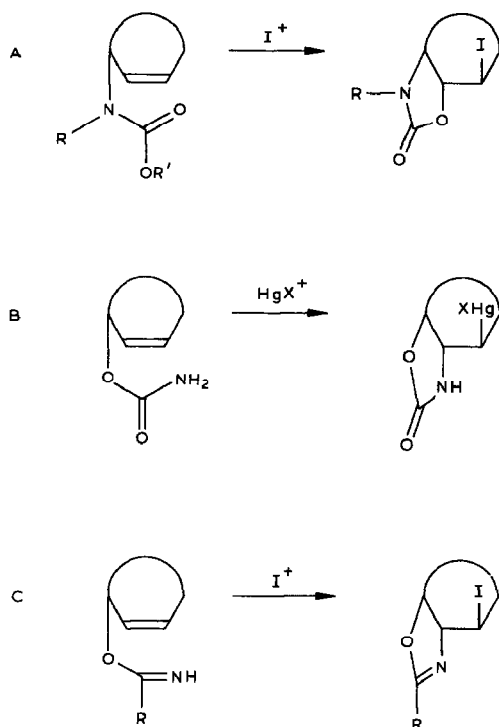
2a X = NH₂, R = R' = H

2b X = NHAc, R = H, R' = Me

2c X = NHAc, R = Ac, R' = Me

*Dedicated to Professor N. K. Kochetkov.

**Taken in part from the Ph.D. Thesis of H.W.P., Duke University, 1984. Present address: Syntex Inc., Mississauga, Ontario, Canada.



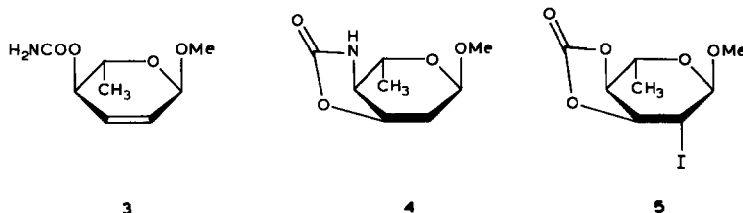
Scheme 1.

However, certain *cis*-hydroxyamino sugars, such as ristosamine (**1a**) and daunosamine (**2a**), are not amenable to this approach, because the required unsaturated sugars (which would be hex-4-enopyranosides) are not readily available. Ristosamine, a subunit of the cyclopeptide antibiotics ristocetin⁶ and avoparcin⁷, was first synthesized in 1975^{8,9}. Its more celebrated isomer, daunosamine, is the glycosidic component of the clinically important antitumor agents daunomycin and adriamycin¹⁰. Interest in the preparation of daunosamine has remained strong¹¹⁻¹⁵ since its isolation in 1964. Synthesis of these biologically important sugars would be simplified if a complementary procedure were developed, in which nitrogen is the nucleophilic species, and the allylic oxygen imposes the necessary stereochemical constraints. Two types of functional groups were considered, namely, primary urethanes (Scheme 1B) and imidates (Scheme 1C). We now describe the development of such a reaction (Scheme 1C) and its application to the syntheses of protected forms of ristosamine¹⁶ (**1b**) and daunosamine¹⁷ (**2b**).

RESULTS AND DISCUSSION

Our original approach to ristosamine sought to utilize the primary allylic urethane methyl 4-*O*-carbamoyl-2,3,6-trideoxy- α -*L*-threo-hex-2-enopyranoside (**3**).

Primary urethanes add *inter*-molecularly to alkenes *via* nitrogen in the presence of mercuric ion¹⁸. An *intra*-molecular version of this reaction followed by borohydride reduction should yield the cyclic carbamate **4** having the desired *cis*-hydroxyamino relationship.

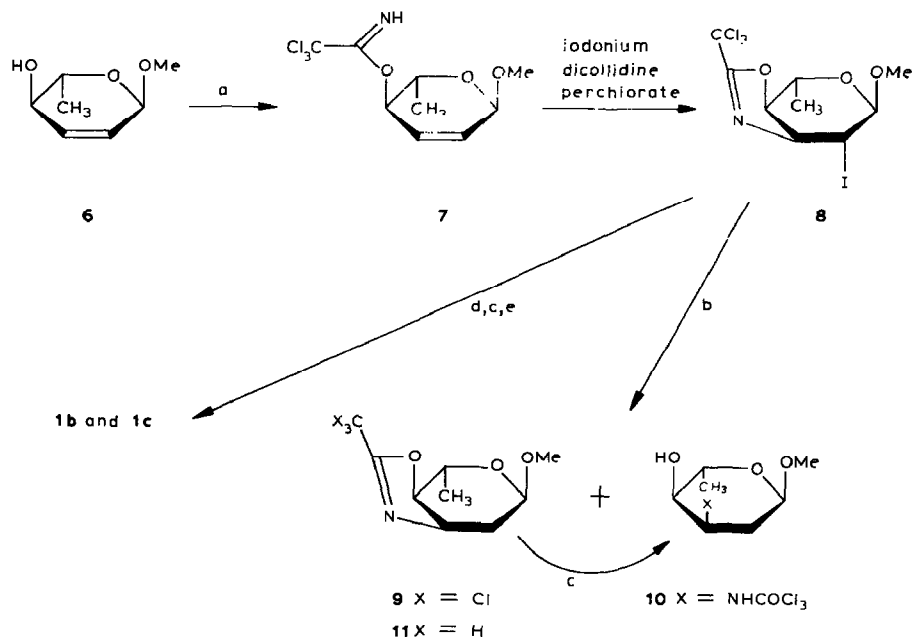


Accordingly, **3**¹⁹ was treated with mercuric nitrate. All of the urethane was consumed (t.l.c.), but reduction of the highly polar adduct regenerated **3**. Although the "polar adduct" was not fully characterized, it appeared to involve complexation of the mercuric ion and the urethane function. Interestingly, **3** reacted readily when iodonium dicollidine perchlorate²⁰ was the electrophile, but the product was the carbonate **5**, not the desired carbamate. A full account of this and related reactions has been published¹⁹.

We then turned to the concept in Scheme 1C involving the use of an allylic imidate which has the advantage of containing only one nucleophilic center, *i.e.*, the nitrogen. Several trichloroacetimidate-containing sugars have been described²¹ and a modification of Overman's procedure²² was used for the reaction with methyl 2,3,6-trideoxy- α -L-erythro-hex-2-enopyranoside (**6**). The resulting crude imidate **7** was treated, without purification, with iodonium dicollidine perchlorate to give the iodo-oxazoline **8**, indicating that the nucleophilicity of the nitrogen had not been decreased substantially by the electron-withdrawing trichloromethyl group. Unfortunately, it was not possible to deiodinate **8** selectively²³ without affecting the trichloromethyl group. Over-reduction and hydrolysis of the oxazoline were interfering reactions.

Treatment of **8** with tributyltin hydride gave the oxazoline **9** and the amide **10** as two major products. The conversion **9**→**10** occurred on storage at room temperature for several days, or by heating in aqueous pyridine with toluene-*p*-sulfonic acid. However, there were several partially chlorinated products which lowered the overall yield of **10**.

This problem was circumvented by using an excess of tributyltin hydride. The expected oxazoline **11** could be isolated by chromatography, but the preferred course was to hydrolyze the crude material and thereby obtain **1b** directly. This procedure also eliminated losses due to the hydrolysis of **11**. The *N*-acetyl derivative **1b** was converted into the diacetyl derivative **1c**, which was identical to authentic methyl di-*N,O*-acetyl- α -L-ristosaminide⁸. After this synthesis appeared in preliminary form¹⁶, the conversion of the iodo-oxazoline **8** into ristosamine **1a** was reported²⁴.

(a) NaH, CCl₃CN

(b) 1.4 equiv. tributyltin hydride

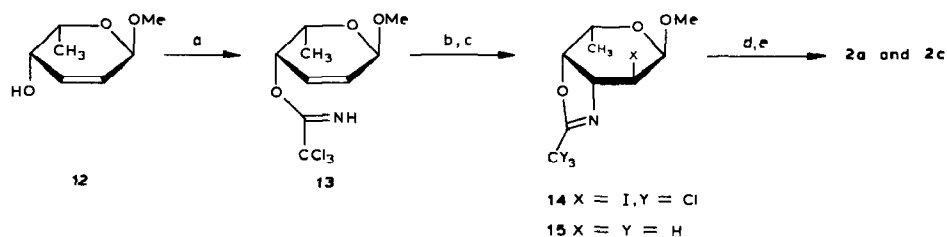
(c) TsOH, pyridine, H₂O

(d) 4.4 equiv. tributyltin hydride

(e) Ac₂O, pyridine

Application of the above sequence to methyl 2,3,6-trideoxy- α -L-threo-hex-2-enopyranoside (**12**), the epimer of **6**, should yield daunosamine. The allylic alcohol **12** was most readily prepared by Mitsunobu inversion²⁵ of **6**. Cardillo *et al.* have reported a moderate yield for this reaction²⁶, but inverse addition of the reactants led to excellent yields. Thus, reaction of **6** and benzoic acid in tetrahydrofuran with the triphenylphosphine-diethylazodicarboxylate complex followed by saponification afforded 89% of **12**¹⁸.

The imidate **13** was prepared readily, but cyclization proceeded much more slowly than for its epimer **7**. It appears that, in **13**, MeO-1 hinders *syn* approach of

(a) NaH, CCl₃CN

(b) Iodonium dicollidine perchlorate

(c) tributyltin hydride

(d) TsOH, pyridine, H₂O(e) Ac₂O, pyridine

the iodonium ion to the double bond. However, after 3 days, 90% of the iodo-oxazoline **14** could be isolated. Reduction of **14** and hydrolysis of the product, as described for **8**, gave methyl *N*-acetyl- α -L-daunosaminide (**2b**). Both **2b** and its diacetyl derivative **2c** had physical constants which agreed with literature values²⁷. The overall yield of methyl *N*-acetyl- α -L-daunosaminide from **6** was 55%.

EXPERIMENTAL

General. — Melting points were determined in capillary tubes with a Buchi 510 melting-point apparatus, and are uncorrected. Elemental analyses were performed by Dr. F. Kasler (Department of Chemistry, University of Maryland) or by M. H. W. Laboratories (P.O. Box 15149, Phoenix, AZ). Optical rotations were determined with a Perkin-Elmer 241 polarimeter. I.r. spectra were recorded with a Perkin-Elmer IR-297 spectrometer, using sodium chloride cells with chloroform as solvent for solids, or sodium chloride plates for films. ¹H-N.m.r. spectra were recorded with Varian EM-360A (60 MHz), Bruker NR-80 (80 MHz), and Varian XL-100 (100 MHz) spectrometers for solutions in CDCl₃ (internal Me₄Si). Coupling constants were obtained by measuring the spacings of the spectra judged to be first order. The progress of all reactions was monitored by t.l.c. on silica gel 60 (HF-254, Merck) with methanol-dichloromethane (*A*, 1:24; *B*, 1:9), or *C*, ethyl acetate-light petroleum (3.5:6.5). The chromatograms were viewed under u.v. light and charred with sulfuric acid. Flash column chromatography²⁹ was performed with Kieselgel 60 (230–400 mesh, Merck).

2-Trichloromethyl-(methyl 2,3,4,6-tetradecoxy-2-iodo- α -L-altropyranosido)-[3,4-d]-2-oxazoline (8). — Methyl 2,3,6-trideoxy- α -L-erythro-hex-2-enopyranoside^{29,30} (**6**; 0.164 g, 1.14 mmol) was dissolved in dry dichloromethane (25 mL), to which was added sodium hydride dispersion in oil (50%; 0.06 g, 1.25 mmol; pre-washed with light petroleum). The mixture was stirred for 30 min at 0°, with the exclusion of moisture, then treated with trichloroacetonitrile (0.12 mL, 1.20 mmol), stirred at 0° for 2 h, and warmed to room temperature. The dichloromethane was evaporated to leave a residue which was partially redissolved in a solution of methanol (0.05 mL, 1.25 mmol) in light petroleum (30 mL). The resulting suspension was agitated briefly, then filtered through Celite, and concentrated to a syrup (crude **7**), which was dissolved in dry acetonitrile (30 mL) and treated with iodonium dicollidine perchlorate²⁰ (0.488 g, 1.31 mmol). The mixture was stirred in the dark for 24 h, the solvent was then removed, and the residue was dissolved in dichloromethane (25 mL). Ether (100 mL) was added, the precipitate was removed, the filtrate was washed with aqueous 10% sodium thiosulfate, aqueous 5% hydrochloric acid, and saturated aqueous sodium hydrogencarbonate, dried, and concentrated. Chromatography (solvent *A*) yielded **8** (0.358 g, 76%), which was recrystallized from light petroleum to give white needles, m.p. 142–143°, [α]_D²³ +23° (c 0.4, chloroform), *R*_F 0.69 (solvent *A*); $\nu_{\max}^{\text{CHCl}_3}$ 3400 (NH), 1660 (C=N), 1448, 1398, 1290 cm⁻¹. ¹H-N.m.r. data (60 MHz, CDCl₃): δ 1.40 (d, 3 H, *J*_{5,6} 6.0 Hz,

CH₃), 3.44 (s, 3 H, OMe), 3.70–4.30 (m, 2 H, H-2,5), 4.48 (d, 1 H, $J_{2,3}$ 1.0, $J_{3,4}$ 9.0 Hz, H-3), 4.74 (dd, 1 H, $J_{4,5}$ 5.3 Hz, H-4), 5.04 (d, 1 H, $J_{1,2}$ 6.3 Hz, H-1).

Anal. Calc. for C₉H₁₁Cl₃INO₃: C, 26.08; H, 2.68; N, 3.38. Found: C, 26.29; H, 2.70; N, 3.32.

A chromatographed (solvent A) sample of the imidate **7** from a separate experiment showed R_F 0.64 (solvent A); $\nu_{\max}^{\text{CHCl}_3}$ 3345 (N=H), 1660 (C=N) cm⁻¹. ¹H-N.m.r. data (60 MHz, CDCl₃): δ 1.35 (d, 3 H, $J_{5,6}$ 6 Hz, CH₃), 3.45 (s, 3 H, OMe), 4.10 (dq, 1 H, $J_{4,5}$ 9.0 Hz, H-5), 4.89 (bs, 1 H, H-1), 5.19 (bd, 1 H, H-4), 5.66–6.23 (m, 2 H, $J_{2,3}$ 10.6 Hz, H-2,3), 8.48 (bs, 1 H, NH).

Methyl N-trichloroacetyl- α -L-ristosaminide (10). — (a) Tributyltin hydride (0.54 mL, 0.203 mmol) was added dropwise (30 min) to a refluxing solution of **8** (0.060 g, 0.145 mmol) and azobisisobutyronitrile (0.002 g, 0.012 mmol) in dry benzene (25 mL). After **8** had been consumed (~2 h), the solvent was removed, and a solution of the residue in acetonitrile (60 mL) was washed with light petroleum (2 \times 25 mL). T.l.c. then revealed two major products of higher mobility and numerous slower-running products. The major components were isolated by chromatography (solvent C, then A) to yield **9** (0.011 g, 26%) and **10** (0.006 g, 14%).

2-Trichloromethyl-(methyl 2,3,4,6-tetra-deoxy- α -L-altropyranosido)-[3,4-*d*]-2-oxazoline (**9**) had $[\alpha]_D^{23} +51^\circ$ (c 0.35, chloroform), R_F 0.34 (solvent A); $\nu_{\max}^{\text{CHCl}_3}$ 1660 (C=N) cm⁻¹. ¹H-N.m.r. data (100 MHz, CDCl₃): δ 1.39 (d, 3 H, $J_{5,6}$ 6.0 Hz, CH₃), 1.78 (m, 1 H, $J_{1,2a}$ 7.5, $J_{2a,3}$ 9.5 Hz, H-2a), 2.35 (dt, 1 H, $J_{1,2e}$ 6.0, $J_{2e,2a}$ 14.5, $J_{2e,3}$ 6.0 Hz, H-2e), 3.43 (s, 3 H, OMe), 3.99 (m, 1 H, $J_{4,5}$ 8.0 Hz, H-5), 4.28–4.47 (m, 2 H, H-3,4), 4.72 (dd, 1 H, H-1).

Methyl N-trichloroacetyl- α -L-ristosaminide (10) had $[\alpha]_D^{23} +32^\circ$ (c 0.55, chloroform), R_F 0.15 (solvent A); $\nu_{\max}^{\text{CHCl}_3}$ 3470, 3355 (OH, NH), 1730 (C=O) cm⁻¹. ¹H-N.m.r. data (100 MHz, CDCl₃): δ 1.33 (d, 3 H, $J_{5,6}$ 6.0 Hz, CH₃), 2.06 (m, 2 H, H-2a,2e), 2.57 (bs, 1 H, OH), 3.44 (2, 3 H, OMe), 3.45–3.85 (m, 2 H, $J_{4,5}$ 9.5 Hz, H-4,5), 4.43 (m, 1 H, H-3), 4.81 (t, 1 H, H-1), 8.60 (bs, 1 H, NH).

(b) When stored at room temperature, **9** was slowly converted into **10**. This process was accelerated by heating to 100° a solution of **9** (0.027 g, 0.094 mmol) in pyridine (1 mL) and water (0.25 mL) containing toluene-*p*-sulfonic acid monohydrate (0.018 g, 0.094 mmol). After 45 min, excess of sodium hydrogencarbonate was added, the mixture was filtered through Celite, insoluble material was washed with toluene, and the combined filtrate and washings were concentrated to yield **10** (0.035 g, quantitative) with physical constants as described above.

Methyl N-acetyl- α -L-ristosaminide (1b). — To a solution of **8** (0.57 g, 1.38 mmol) in dry benzene (50 mL) was added azobisisobutyronitrile (0.01 g, 0.061 mmol) and tributyltin hydride (1.75 g, 6.07 mmol). The mixture was boiled under reflux for 4 h, and then worked-up as described above to give impure oxazoline **11** which was hydrolyzed as for **9**, but for 90 min. The product obtained was chromatographed (solvent A) to give methyl *N*-acetyl- α -L-ristosaminide (**1b**) (0.139 g, 50%, 2 steps) as a syrup, $[\alpha]_D^{23} -27^\circ$ (c 1.3, chloroform), R_F 0.41 (solvent A);

$\nu_{\max}^{\text{CHCl}_3}$ 3400 (NH, OH), 1655 (C=O) cm^{-1} . $^1\text{H-N.m.r.}$ data (100 MHz, CDCl_3): δ 1.28 (d, 3 H, $J_{5,6}$ 6.3 Hz, CH_3), 1.87–2.10 (m, 2 H, H-2a, 2e), 2.05 (s, 3 H, Ac), 3.40 (s, 3 H, OMe), 3.35–3.65 (m, 1 H, $J_{3,4}$ 4.0 Hz, H-4), 3.84 (dq, 1 H, $J_{4,5}$ 9.0 Hz, H-5), 4.18 (bs, 1 H, OH), 4.51 (m, 1 H, H-3), 4.73 (bs, 1 H, H-1), 7.15 (bs, 1 H, NH).

Anal. Calc. for $\text{C}_9\text{H}_{17}\text{NO}_4$: C, 53.19; H, 8.43; N, 6.89. Found: C, 52.97; H, 8.44; N, 6.88.

In a separate experiment, a chromatographed sample of 2-methyl-(methyl 2,3,4,6-tetradecoxy- α -L-altropyranosido)-[3,4-*d*]-2-oxazoline (**11**) had $[\alpha]_D^{23} +74^\circ$ (c 25, chloroform), R_F 0.44 (solvent B). $^1\text{H-N.m.r.}$ data (60 MHz, CDCl_3): δ 1.32 (d, 3 H, $J_{5,6}$ 5.7 Hz, CH_3), 1.50–2.50 (m, 2 H, H-2a, 2e), 1.96 (s, 3 H, OCNMe), 3.40 (s, 3 H, OMe), 3.65–4.28 (m, 3 H, H-3, 4, 5), 4.70 (dd, 1 H, $J_{1,2e}$ 5.5, $J_{1,2a}$ 8.0 Hz, H-1).

Methyl di-N,O-acetyl- α -L-ristosaminide (1c). — To a solution of **1b** (0.025 g, 0.124 mmol) in dry pyridine (3 mL) was added acetic anhydride (0.50 mL, 5.3 mmol). The mixture was stirred at room temperature for 4 h with the exclusion of moisture, then diluted with toluene (20 mL), and concentrated to dryness to give amorphous **1c** (0.027 g, 90%), which was identical (t.l.c., i.r. and $^1\text{H-n.m.r.}$ spectra) to the authentic material; $[\alpha]_D^{23} -141^\circ$ (c 0.35, chloroform) [lit.⁸ $[\alpha]_D^{21} -134^\circ$ (c 0.5, chloroform)], R_F 0.21 (solvent A); $\nu_{\max}^{\text{CHCl}_3}$ 3400 (NH), 2940, 1745 (ester C=O), 1675 (amide C=O), 1510, 1365, 1230, 1125, 1050 cm^{-1} . $^1\text{H-N.m.r.}$ data (100 MHz, CDCl_3): δ 1.21 (d, 3 H, $J_{5,6}$ 6.0 Hz, CH_3), 1.74–2.10 (m, 2 H, H-2e, 2a), 1.99, 2.01 (2 s, 6 H, NAc and OAc), 3.42 (s, 3 H, OMe), 3.92 (dq, 1 H, $J_{4,5}$ 10.0 Hz, H-5), 4.46–4.69 (m, 2 H, $J_{3,4}$ 3.7 Hz, H-3, 4), 4.74 (bd, 1 H, $J_{1,2e}$ 3.0 Hz, H-1), 6.80 (bd, 1 H, NH).

*2-Trichloromethyl-(methyl 2,3,4,6-tetradecoxy-2-iodo- α -L-galactopyranosido)-[3,4-*d*]-2-oxazoline (14).* — Methyl 2,3,6-trideoxy- α -L-threo-hex-2-enopyranoside (**12**; 0.5 g, 3.47 mmol) was treated with sodium hydride (50% dispersion in oil; 0.183 g, 3.81 mmol) and trichloroacetonitrile (0.35 mL, 3.50 mmol) as described for the preparation of **7**. The work-up was performed quickly to yield the imidate **13** as a syrup, which was treated immediately with iodonium ion as described for **8** (3 equiv. of iodonium dicollidine perchlorate for 3 days), to give **14** (1.29 g, 90%), m.p. 151–152.5° (from light petroleum), $[\alpha]_D^{23} -124^\circ$ (c 1.1 chloroform), R_F 0.70 (solvent A); $\nu_{\max}^{\text{CHCl}_3}$ 3020, 1650 (C=N), 1445, 1363 cm^{-1} . $^1\text{H-N.m.r.}$ data (80 MHz, CDCl_3): δ 1.38 (d, 3 H, $J_{5,6}$ 6.7 Hz, CH_3), 3.47 (s, 3 H, OMe), 3.88 (dd, 1 H, $J_{1,2}$ 3.8, $J_{2,3}$ 7.8 Hz, H-2), 4.14–4.85 (m, 4 H, $J_{4,5}$ 2.0 Hz, H-1, 3, 4, 5).

Anal. Calc. for $\text{C}_9\text{H}_{11}\text{Cl}_3\text{INO}_3$: C, 26.08; H, 2.68; N, 3.38. Found: C, 26.33; H, 2.67; N, 3.53.

In a separate experiment, a purified sample of **13** had $[\alpha]_D^{23} -75^\circ$ (c 0.45, chloroform), R_F 0.65 (solvent A); $\nu_{\max}^{\text{CHCl}_3}$ 3360 (NH), 1670 (C=N), 1295, 1200, 1050, 800 cm^{-1} . $^1\text{H-N.m.r.}$ data (100 MHz, CDCl_3): δ 1.24 (d, 3 H, CH_3 , $J_{5,6}$ 6.9 Hz, CH_3), 3.42 (s, 3 H, OMe), 4.28 (qd, 1 H, $J_{4,5}$ 2.4 Hz, H-5), 4.90–5.10 (m, 2 H, H-1, 4), 6.02 (dd, 1 H, $J_{1,2}$ 2.5, $J_{2,3}$ 10 Hz, H-2), 6.27 (dd, 1 H, $J_{3,4}$ 4.7 Hz, H-3).

Methyl N-acetyl- (2b) and di-N,O-acetyl- α -L-daunosaminide (2c). — Compound **14** (1.29 g, 3.11 mmol) was reduced and hydrolyzed as described for the preparation of **1b**, to yield **2b** (0.476 g, 75%), m.p. 179–180° (from ethyl acetate), $[\alpha]_D^{23} -230^\circ$ (*c* 1, methanol), R_F 0.21 (solvent *B*); $\nu_{\max}^{\text{CHCl}_3}$ 3370 (NH, OH), 1700 (C=O), 1560, 1305, 1155, 1110, 1045 cm^{-1} . $^1\text{H-N.m.r.}$ data (60 MHz, CDCl_3): δ 1.21 (d, 3 H, $J_{5,6}$ 6.1 Hz, CH_3), 1.80 (m, 2 H, H-2a,2e), 1.96 (s, 3 H, NAc), 3.34 (s, 3 H, OMe), 3.38–3.66 (m, 2 H, H-4, OH), 3.96 (bq, 1 H, $J_{4,5}$ 1 Hz, H-5), 4.32 (m, 1 H, H-3), 4.72 (bs, 1 H, H-1), 6.52 (bs, 1 H, NH).

In a separate experiment, a chromatographed sample of 2-methyl-(methyl 2,3,4,6-tetra-deoxy- α -L-galactopyranosido)-[3,4-*d*]-2-oxazoline (**15**) had $[\alpha]_D^{23} -115^\circ$ (*c* 0.75, chloroform), R_F 0.38 (solvent *B*); $\nu_{\max}^{\text{CHCl}_3}$ 1670 (C=N), 1460, 1385, 1040 cm^{-1} . $^1\text{H-N.m.r.}$ data (80 MHz, CDCl_3): δ 1.16 (d, 3 H, $J_{5,6}$ 6.3 Hz, CH_3), 1.33–1.80 (m, 1 H, H-2a), 1.89 (s, 3 H, OMe), 2.21 (bdd, 1 H, $J_{2a,2e}$ 13.5, $J_{1,2e}$ 5.5 Hz, H-2e), 3.27 (s, 3 H, OMe), 3.83 (q, 1 H, H-5), 4.25 (bs, 2 H, H-3,4), 4.58 (dd, 1 H, $J_{1,2a} = 7.6$ Hz, H-1).

The diacetate **2c** (prepared as described for **1c**) had m.p. 186–187° (from ethyl acetate), $[\alpha]_D^{23} -208^\circ$ (*c* 1, chloroform) {lit.²⁸ m.p. 188–189°, $[\alpha]_D -202^\circ$ (*c* 1, chloroform)}, R_F 0.40 (solvent *B*). $^1\text{H-N.m.r.}$ data (60 MHz, CDCl_3): δ 1.10 (d, 3 H, $J_{5,6}$ 6.5 Hz, CH_3), 1.47–2.00 (m, 2 H, H-2a,2e), 1.92 (s, 3 H, NAc), 2.19 (s, 3 H, OAc), 3.36 (s, 3 H, OMe), 4.04 (q, 1 H, $J_{4,5}$ 1 Hz, H-5), 4.46 (m, 1 H, H-3), 4.80 (bs, 1 H, H-1), 5.07 (d, 1 H, $J_{3,4}$ 2.0 Hz, H-4), 6.79 (d, 1 H, $J_{\text{NH},3}$ 8.0 Hz, NH).

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