Since the above comparison proves the identity of the natural and synthetic ristosamine and derivatives, the structure of ristosamine as 3-amino-2,3,6-trideoxy-L-*ribo*-hexopyranose is confirmed.

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(9) TLC was run on silica gel plates and visualized by $H_2SO_4$ spray.
(10) Compare the case of natural and synthetic methyl *N,O*-diacetyl-α-daunosaminide. See ref 1b, footnote 9.
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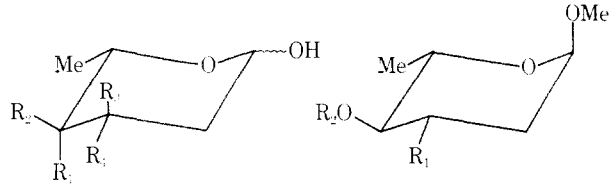
## Confirmation by Synthesis of the Structure of Acosamine and Methyl *N*-Acetylactinosaminide

*Sir:*

The accompanying communication[1] reports the synthesis of ristosamine, 3-amino-2,3,6-trideoxy-L-*ribo*-hexose, and the reasons for our interest in this family of amino sugars. In this manuscript we report the synthesis of 3-amino-2,3,6-trideoxy-L-*arabino*-hexose[2] and confirmation of its structural assignment to acosamine,[3] a component of the antibiotic, actinodin. Thus it is now feasible to replace the sugar moiety of adriamycin, daunosamine, with two other closely related sugars in efforts to modify the antitumor properties of adriamycin.[4] In addition, this manuscript describes the preparation of the methyl glycoside of 3-amino-4-*O*-methyl-2,3,6-trideoxy-L-*arabino*-hexose and confirmation of its assignment, by Lomakina et al.,[3] to methyl actinosaminide, a compound derived by methanolysis of actinoidin.




1. $R_2$ = OH; $R_3$ = $NH_2$
2. $R_2$ = OMe; $R_3$ = $NH_2$
3. $R_1$ = OH; $R_3$ = $NH_2$
4. $R_2$ = OH; $R_3$ = $NH_2$
other R's = H

5. $R_1$ = $N_3$; $R_2$ = H
6. $R_1$ = $NH_2$; $R_2$ = H
7. $R_1$ = NHAc; $R_2$ = H
8. $R_1$ = NHAc; $R_2$ = Ac
9. $R_1$ = NHAc; $R_2$ = Me
10. $R_1$ = NMeAc; $R_2$ = Me

Catalytic hydrogenation of methyl 3-azido-2,3,6-trideoxy-α-L-*arabino*-hexopyranoside (**5**), an intermediate in the synthesis of daunosamine,[5] afforded the amino **6**[6] in high yields with properties [mp 130–132° (benzene–hexane); $[\alpha]^{21}D$ −144° (*c* 0.52, MeOH); $R_f$ 0.2 in $C_6H_6$–MeOH (4:1)][7] agreeing well with those previously reported[2] and less well with the rotation of methyl acosaminide, $[\alpha]^{20}D$ −118° (*c* 0.5, MeOH).[3,8] Heating **6** in 0.2 *N* HCl for 90 min at 90–95° followed by partial neutralization and lyophilization at pH 5.8 afforded high yields of the hydrochloride of 3-amino-2,3,6-trideoxy-L-*arabino*-hexopyranose,[6] analyzing for $1\cdot HCl\cdot \frac{1}{3}H_2O$, $[\alpha]^{21}D$ −18.3° (*c* 0.43, $H_2O$) at equilibrium.

Reaction of **6** with acetic anhydride in anhydrous methanol and in pyridine gave a quantitative yield of the *N*-acetyl **7** and 71% yield of the *N,O*-diacetyl **8**, respectively. Recrystallization from MeOH–ether afforded the analytically pure **7**[6] [mp 160–161°; $[\alpha]^{21}D$ −146° (*c* 0.52, MeOH); $R_f$ 0.3 in benzene–methanol (4:1)] as compared to those reported for methyl *N*-acetylacosaminide [mp 161–162° (chloroform–ether); $[\alpha]^{20}D$ −90° (*c* 0.1, methanol)][3,8] and for the previously prepared **7**[2] [mp 159–160° (ether–petroleum ether); $[\alpha]^{20}D$ −148° (*c* 0.4, methanol)]. Recrystallization of **8** from ether–petroleum ether (bp 60–110°) yielded the analytically pure methyl *N,O*-diacetyl-3-amino-2,3,6-trideoxy-α-L-*arabino*-hexopyranoside (**8**):[6] mp 163–164°; $[\alpha]^{22}D$ −191° (*c* 0.52, MeOH). For methyl *N,O*-acetylacosaminide, the reported values[3] are mp 158–163° and $[\alpha]^{20}D$ −84° (*c* 0.5, MeOH); the rotation is again less negative.[8]

Methylation of **7** with dimethyl sulfate under the reported conditions[3] did not give the expected **9**, but two other products that mass spectral data suggested may be the dimethylated **10** and a dimeric compound. A different methylation procedure employing silver oxide and excess methyl iodide as solvent[11] afforded **9** [mp 188–190°; $[\alpha]^{21}D$ −150° (*c* 0.5%, MeOH)] as compared to methyl *N*-acetylactinosaminide (**M**) [reported mp 156–158° (ether–*n*-hexane), $[\alpha]^{20}D$ −70° (*c* 0.4, MeOH) when prepared from methyl *N*-acetylacosaminide; and mp 165–168° (chloroform–ether), $[\alpha]^{20}D$ −101° (*c* 0.6, MeOH) when prepared from methyl actinosaminide] but whose other properties (ir and NMR) were identical.[3] These reported results again may result from a difference in anomeric content[8] and, possibly, the presence of some dimethylated **10** in one case.

A comparison has been made of our NMR data and the data and figure reported for methyl *N*-acetylactinosaminide.[3] Its spectrum is reported to differ only by one methyl group[3] from that of methyl *N*-acetylacosaminide (details not reported except δ 3.30 for $C_1$-OMe). The data for **6–9** and **M** are tabulated in Table I. There is complete agreement between our results and the literature results. For all

**Table I.** NMR Data (100 MHz, $DCCl_3$) for 3-Amino-2,3,6-trideoxy-L-*arabino*-hexopyranose Derivatives

| | Chemical shifts and multiplicities[a,b] | | | | | | |
|---|---|---|---|---|---|---|---|
| | H-1 | H-$2_{ax}$ | H-$2_{eq}$ | H-3 | H-4 | H-5 | H-6 |
| **6**[c] | 4.66, dd | 1.50, dq | 2.00, dq | 3.00, dq | 2.83, t | 3.61, dq | 1.26, d |
| **7**[d] | 4.69, dd | 1.63, dt | 2.06, dq | 4.10, m | 3.04, t | 3.67, dq | 1.24, d |
| **8** | 4.70, dd | 1.61, dq | 2.22, dq | 4.42, m | 4.50, t | 3.88, dq | 1.21, d |
| **9** | 4.63, dd | 1.73, dt | 2.09, dq | 4.16, m | 2.88, t | 3.72, dq | 1.25, d |
| M[e] | 4.65, d | 1.73, dt | | 4.25, m | 2.86, t | 3.72, dq | 1.28, d |
| | Coupling constants, $J$, in Hz | | | | | | |
| | $1,2_{ax}$ | $1,2_{eq}$ | $2_{ax},2_{eq}$ | $2_{ax},3$ | $2_{eq},3$ | 3,4 | 4,5 | 5,6 |
| **6**[c] | 3.5 | 1 | 13 | 11.5 | 4.5 | 9 | 9 | 6 |
| **7**[d] | 3.5 | 1 | 12.5 | 12.5 | 4 | 9.5 | 9 | 6.5 |
| **8** | 3.5 | 1.5 | 13 | 10 | 4.5 | 9 | | 6 |
| **9** | 3.5 | 2.0 | 13 | 12 | 5 | 9 | 9 | 6.5 |
| M[e] | ~2–3 | ~2–3 | 12 | 12 | | 10 | | 6.5 |

[a] Chemical shifts are given in δ values relative to $Me_4Si$. Multiplicities are indicated by the usual symbols: d = doublet, dd = double of doublets, t = triplet, q = quartet, m = multiplet. [b] Not shown are the 1-$OCH_3$ singlets at δ 3.32, 3.33, 3.34, 3.31, and 3.28 for compounds **6**–**9** and M, respectively; the 3-NAc singlets at δ 2.00, 1.90, 1.96, and 1.97 for **7**–**9** and M; the 4-OAc singlet at δ 2.05 for **8**; the 4-$OCH_3$ singlets at δ 3.42 and 3.43 for **9** and M; and the NH at δ 6.08 and 5.69 for **7** and **8**. The 1-$OCH_3$ singlet is at δ 3.30 for M. [c] Half of the H-$2_{eq}$ dq was hidden by the NH, OH peak at δ 2.13 (br s) until exchanged by $D_2O$. H-3 and H-4 are overlapped; however, H-3 can be designated as a doublet of quartets centered at δ 3.00 if one extraneous spike (impurity) at δ 2.90 in the overlapped area can be ignored. Otherwise, it also should be designated as a multiplet. [d] One quartet of H-$2_{eq}$ dq hidden by NAc at room temperature. At 60°, one doublet of this hidden quartet was resolved. [e] M is methyl *N*-acetylactinosaminide from natural sources.[3]

the compounds in Table I, the data established unequivocally the arabino configuration and the conformation shown in the formulas. The presence of four consecutive trans-diaxial protons, H-$2_{ax}$–H-5, with their large coupling constants, permits no other interpretation. Our reported spectra, obtained at 60°, had better resolution then the room temperature spectra (ours and the literature ones[3]). For example, all the H-1 protons appear to be a broadened doublet in all the compounds in Table I and are so designated with $J_{1,2_{eq}} \approx J_{1,2} \approx J_{2,3}$ for methyl *N*-acetylactinosaminide. However, we can confidently designate H-1 as a doublet of doublets for **6**–**9** because of the improved resolution of the H-$2_{eq}$ and H-$2_{ax}$ signals when the values of $J_{1,2_{ax}}$ = 3.5 Hz and $J_{1,2_{eq}}$ = 1–1.5 Hz can be measured. Outside of this one difference in designation, the spectra of **9** and methyl *N*-acetylactinosaminide are identical, as can be seen by comparing the data in Table I and also Figure 2 of ref 3 with our spectra. Also, **7** shows the great similarity to **9** that is reported to be shown by methyl *N*-acetylacosaminide to methyl *N*-acetylactinosaminide.

On the basis of the NMR data and the melting point data for the various derivatives, we confirmed by synthesis the earlier assignment[1] of the structures of acosamine as 3-amino-2,3,6-trideoxy-L-*arabino*-hexose (**1**) and methyl *N*-acetylactinosaminide as **9**. The differences in optical rotations of the synthetic and natural acosamine and actinosamine derivatives can most likely be accommodated by differences in anomeric composition.[8]

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(8) The less negative rotations of methyl acosaminide and its *N*-acetyl and *N,O*-diacetyl derivatives as compared to the synthetic **6**–**8** are most probably due to a difference in anomer composition arising from the preparation of methyl acosaminide by acid methanolysis.[3] A similar case of differences in rotations was observed for the originally reported methyl *N,O*-diacetyldaunosaminide from natural sources[9] as compared to the synthetic.[5] The difference was eliminated when the natural source sample was freed of the β anomer.[10]
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