talo-configurations. The latter was in fact obtained as a major product through neighboring participation of the amido function. Thus, the two compounds **87** and **90** were provided by direct nucleophilic substitution and by preferential opening of the acetoxonium ion, respectively.

Compound **87** was *O*-deacetylated with methanolic sodium methoxide (→ **86**) and the diol obtained was again protected with a benzyl group (→ **88**). Then removal of the isopropylidene group generated the 1,2-unprotected derivative **91**. Removal of the benzyl groups of **91** by hydrogenolysis in EtOH in the presence of Pd/C and subsequent hydrolysis with aqueous $Ba(OH)_2$ gave 5-amino-5-deoxy-L-*talo*-quercitol **73** quantitatively. Then, selective methylation of **91** was carried out with 2 M equiv. of CH_3I in MeCN in the presence of Ag_2O at reflux temperature. The mixture of products was fractionated over a silica gel column to give a mixture (52%) of two monomethyl derivatives, **92** and **93**, and one dimethyl form, **94** (33%). The former mixture was conventionally acetylated to give the acetyl derivatives, which were separable on a silica gel column to give **92** (34%) and **93** (49%). Compounds **92**–**94** were deprotected, followed by hydrolysis, affording the corresponding free bases **74** and **75a**,**b**.

Data for inhibitory activity of compounds **73**, **74**, and **75a**,**b** toward three glycosidases are summarized in Table 1. Compounds **74** and **75a** possessed moderate inhibitory activity against α-fucosidase (bovine kidney), while the free base **73** and the dimethyl ether **75b** did not show any such potential. Interestingly, compound **75a** showed cross-inhibitory action toward α-galactosidase (green coffee beans). Thus, the present study demonstrated that methyloxy groups are likely to function as equivalents of the hydrophobic 5-methyl branching in **71a** and/or **71b**, allowing us to design deoxyinosamine-type glycosidase inhibitors other than α-fucosidase. From the present results we therefore propose incorporation of methyl ether groups as one effective route for application of chemically modified inositols as derivatives of biological interest.

In continuation of our biochemical interest in isomeric deoxyinosamines, readily accessible stereoisomers configurationally related to galacto, gluco, and mannopyranosylamines **95**–**98** (Fig. 17) were synthesized and their glycosidase inhibitory activity was assayed. Treatment of **8b** with an excess of NaN_3 in aqueous 90% MCS at

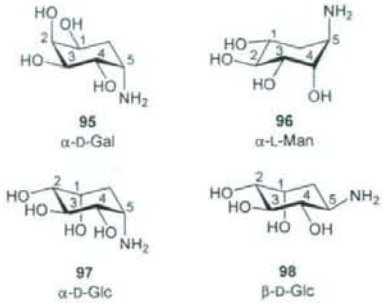

Fig. 17. Four deoxyinosamines structurally related to D-galacto, D-gluco, and L-mannopyranosylamines.

Table 1. Data for inhibitory activity of 5-amino-5-deoxy-L-*talo*-quercitol **(73)** and its methyl ethers **73-75a,b** against three glycosidases: ref. 5a-carba-L fucopyranosylamine **(72)**.

Compound	IC_{50} (μM)		
	α-Fucosidase (bovine kidney)	α-Galactosidase (green coffee beans)	β-Glucosaminidase (bovine kidney)
72	9.3	NI	NI
73	NI	490	NI
74	23	NI	NI
75a	100	20	400
75b	NI	NI	NI

NI: no inhibition; Compound **72** was observed to exhibit strong activity (K_i = 0.12 μM) against α-fucosidase (bovine kidney).

reflux temperature afforded a sole azide **99a** (91%), which was subsequently reduced in the presence of Raney nickel to give, after acetylation, the *N*-acetyl derivative **99b** (84%). Although in general direct S_N2 reactions proceed smoothly in aprotic solvents such as DMF and DMSO, azidolysis was carried out successfully, suppressing possible elimination reactions in a protic solvent at low temperature. Conventional acid hydrolysis of **99b** afforded the free base **95** (ca. 100%) (Fig. 18).

Similarly, starting from the tosylate **10b**, the free base **96** was obtained through azidolysis [→ **100a** (48%)] and reduction followed by acetylation [→ **100b** (91%)]. The yield of **100a** was rather low due to side elimination reactions. Also, the free base **97** was prepared from the tosylated **11b** (→ **101a,b** → **97**). On the other hand, with azidolysis of the deprotected tosylate **35** under similar conditions, neighboring group participation was mainly undergone through formation of an acetoxonium ion, followed by preferential diequatorial-opening by azide anion, to give the azide **102a** (91%). Similar reduction, followed by acetylation, gave compound **102b** (ca. 100%), from which the free base **98** was obtained.

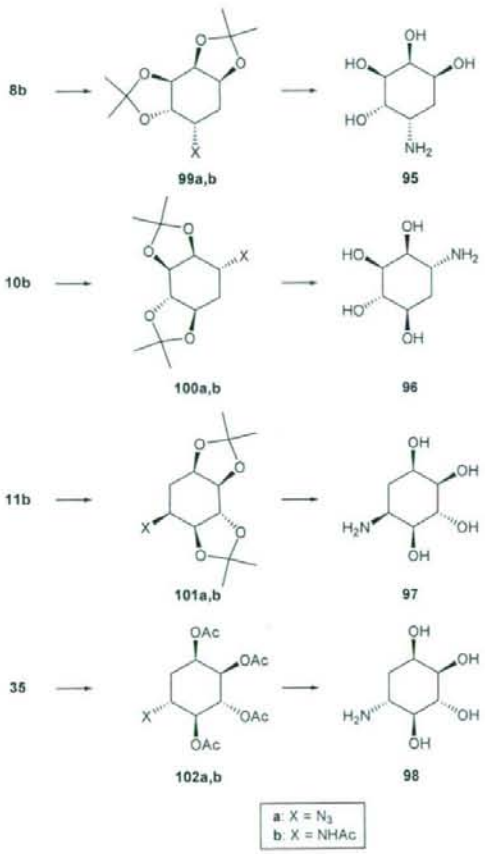

Fig. 18. Synthesis of four biologically interesting deoxyinosamines from (–)-*vibo*-quercitol.

Table 2. Data for inhibitory activity of **95-98** against five glycohydrolases.

Compound	*I*(%)		
	α-Glc[a]	α -Gal[b]	α -Gal[c]
95	40	55	74[d]
96	NI	21	NI
97	48	20	NI
98	33	NI	NI

NI: no inhibition; [a]α-glucosidase (yeast); [b]α-galactosidase (coffee beans); [c]α-galactosidase (rat); [d]IC_{50}=0.26 mM. None of the compounds showed any activity against β-galactosidase (bovine liver) and α-mannosidase (Jack beans).

Deoxyinosamines **95**, **97**, and **98** showed weak but detectable inhibition [*I*(%) 40, 48, and 33%, respectively (100 μg/mL)] specific for α-glucosidase (yeast). Compound **95** also possessed weak activity [*I*(%): 55 and 74% (IC_{50} = 0.26 mM)] against α-galactosidase (coffee beans and rat) (Table 2). Although the levels of activity were very low, these results suggest a certain correlation between the 5-amino-2,3,4-triol structures of bioactive deoxyinosamines and the hexopyranosylamines involved in biological systems.

7. CONCLUSION

In 1966, deoxyinositols were first classified by McCasland as pseudo sugars 5a-carbapentopyranoses [22]. According to his proposal, deoxyinosamines should be 5a-carbapentopyranosylamines. Although biologically active compound of this class has so far never

been found in nature, there is a great possibility of developing new types of bioactive compounds, which are simple mimics of pentopyranoses and analogues. In recent years bioconversion of *myo*-inositol has been shown to produce sufficient quantities of optically active deoxyinositols, allowing us to utilize such raw materials easily for design and synthesis of biologically interesting cyclitol derivatives. In this article, focused on preparative examples in line with our future expectations to successful elaboration of new bioactive carbasugars.

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