Synthesis of (1*R*,2*S*,3*R*,4*R*)-2,3,4-Trihydroxycyclopentylamine from D-Ribonolactone

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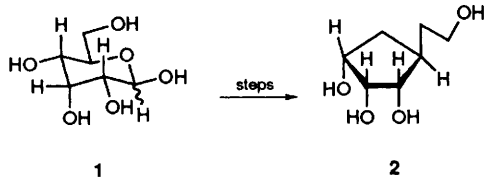
A seven-step procedure for the transformation of ribonolactone **3** into the aminotriol **12** can be effected in 28% overall yield.

Recently we reported the conversion of D-allose **1** into the cyclopentanetetrol **2** using a radical-catalysed cyclization process in the key step (Scheme 1).[1] We now disclose development of this methodology to allow the preparation of an interesting polyhydroxycyclopentylamine (Scheme 2).

D-Ribonolactone **3** was converted into the bromolactone **4** using a prescribed pathway.[2] Treatment of the lactone **4** with diisobutylaluminium hydride (DIBAL-H) followed by *O*-benzylhydroxylamine furnished the oxime **5** as a mixture of *Z*- and *E*-stereoisomers in a ratio of 1 : 2.5 and an overall yield of 74%. To a refluxing solution of this mixture in benzene was added a solution of AIBN and tri-*n*-butyltin hydride over 30 min using a syringe pump. A smooth cyclization took place to afford the bicyclic compound **8** as the sole isolated product (79% yield). The use of a substituted oxime as a radical trap has precedent in the literature.[3] Deprotection of the acetal **8** gave a quantitative yield of the corresponding triol **11** which was reduced (80% yield) to the title aminotriol **12** by hydrogenation using Raney nickel as the catalyst.[4]

The *O*-methyl oxime **6** was prepared from the lactone **4** (75% yield) in a similar manner, again as a mixture of *Z*- and *E*-isomers (1 : 2.4, respectively). This inseparable mixture was cyclised (70% yield) to yield compound **9**. Reduction of this hydroxylamine derivative under the standard conditions[4] afforded the amine **13** (an obvious precursor to 5′-noraristeromycin[5] and analogues) which has the following spectral characteristics: ν_{max} (neat)/cm^{-1} 3355 br s (OH_{str} and NH_{str}), 2987 and 2935 (CH_{str}), 1672 and 1599 (NH_{def}), 1372, 1103 and 1054 ($C–O_{str}$ and $O–H_{def}$). δ_H (300 MHz, CD_3OD): 4.54 (1H, t, *J* 5 Hz, 3-H), 4.34–4.25 (2H, m, 2-H and 4-H), 3.21 (1H, dt, *J* 6 and 0.6 Hz, 1-H), 1.96 (1H, ddd, *J* 12.8, 10.7 and 6 Hz, 5-H), 1.75 (1H, ddd, *J* 12.8, 6 and 0.6 Hz, 5-H), 1.44 (3H, s, Me), 1.31 (3H, s, Me). δ_C (75.47 MHz, CD_3OD): 112.1 (C), 87.1 (CH, C-4), 80.6 (CH, C-3), 72.4 (CH, C-2), 54.8 (CH, C-1), 38.3 (CH_2, C-5), 26.2 (Me), 24.3 (Me).

The efficiency of the synthetic route from D-ribonolactone to the amines **12** and **13** depends on the formation of a single diastereoisomer during the radical cyclization reaction. The



1 **2**

Scheme 1

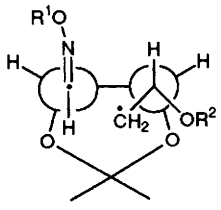
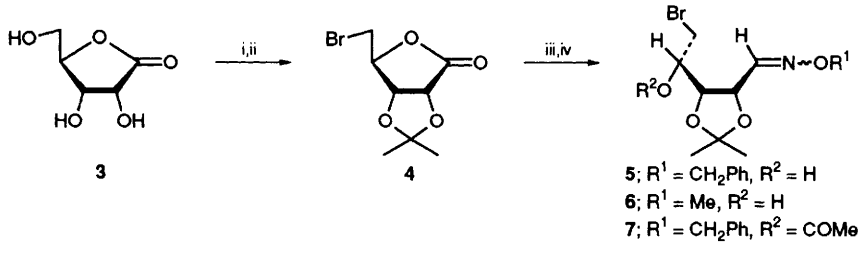
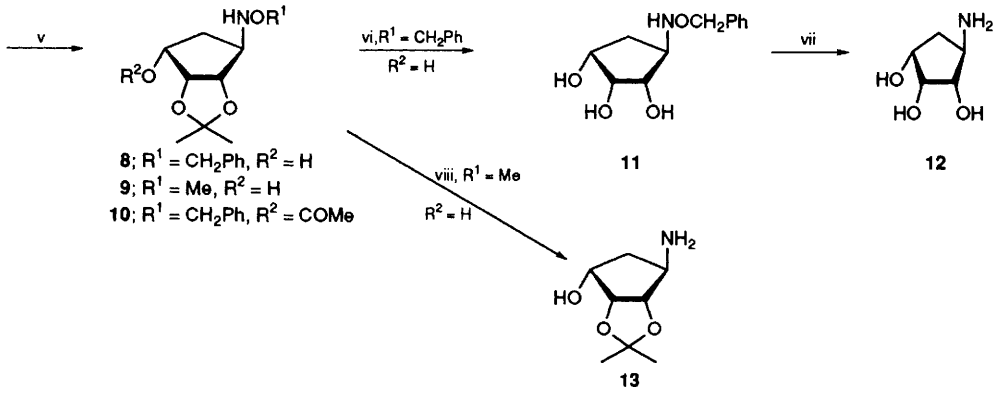


Fig. 1



3 **4**



11 **12**

13

Scheme 2. *Reagents and conditions*: i, conc. H_2SO_4 (cat.), acetone, room temp., 5 h; ii, NBS, Ph_3P, CH_2Cl_2, room temp., 2 h; iii, DIBAL-H, toluene, −78 °C, 2 h; iv, NH_2OR^1 HCl, pyridine, CH_2Cl_2, room temp., 16 h; v, AIBN (0.26 equiv.), Bu_3SnH (2.14 equiv.), benzene, 80 °C, 1.5–4.5 h; vi, 1 mol dm^{-3} HCl, THF (1 : 1), room temp., 1 h; vii, H_2, Raney Ni, EtOH, 40 °C, 3 days; viii, H_2, Raney Ni, EtOH, 40 °C, 1 h (60%); NBS = *N*-bromosuccinimide

preferred conformation of the radical intermediate must be independent of the stereochemistry of the oxime moiety and one possible candidate is shown in Fig. 1. The possibility that intramolecular hydrogen bonding between the hydroxy group and the acetonide unit contributes to the selectivity of the ring-closure reaction **5** → **8** was discounted when it was found that the acetate **7** formed the cyclopentane derivative **10** cleanly in 70% yield under the usual conditions.

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