Tetrahedron Letters,Vol.28,No.12,pp 1327-1328,1987   0040-4039/87 $3.00 + .00
Printed in Great Britain   Pergamon Journals Ltd.

SYNTHESIS OF L-DAUNOSAMINE FROM D-GLUCURONO-6,3-LACTONE

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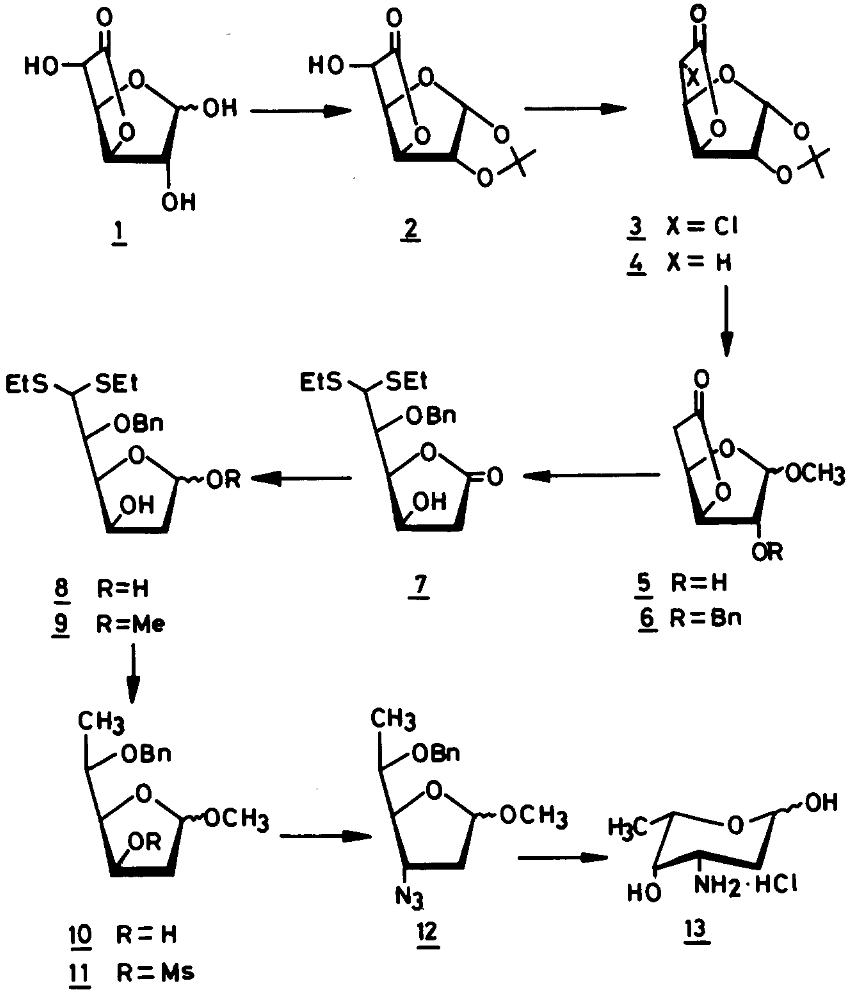
Summary:- L-Daunosamine has been synthesised from D-Glucurono-6,3-lactone in which carbon atoms C-6/1 of the lactone are transformed into C-1/6 of aminosugar by a new approach.

Anthracycline antibiotics are the subject[1] of immense interest owing to their clinically useful anticancer activity. The aminosugar (L-daunosamine) present in almost all the anthracyclines has been synthesised from several carbohydrate precursors[2,3]. The common feature observed in all the syntheses is that carbon atoms C-1/6 of the starting sugar moiety remain C-1/6 of daunosamine. However, it was realised that if carbon atoms C-1/6 of D-Glucose are transformed into C-6/1 of daunosamine, then the crucial step of epimerisation at C-5 could be curtailed. Herein we report a new approach for the synthesis of L-daunosamine.

Commercially available D-Glucurono-6,3-lactone (1) (obtained from D-glucose) was protected as 1,2-isopropylidene derivative (2)[4]. Introduction of the chlorine atom at C-5 was effected[5] with sulfuryl chloride-pyridine to afford 3 which on reductive dechlorination with tri-n-butyltin hydride and catalytic amount of AIBN in refluxing toluene gave the 5-deoxy product (4)[6] in overall 87% yield. Treatment of 4 with dry methanol and Amberlite IR 120 (H) resin under reflux gave a mixture of α,β-glycosides (5), the free hydroxyl group of which was protected as benzyl ether by the reaction with benzyl bromide and silver oxide in benzene to give 6 (54%).

Compound 6 and ethanethiol in the presence of conc. hydrochloric acid then afforded the diethylmerchaptan derivative 7 which with DIBAL at -78° in methylene chloride gave the hemiacetal 8 (60%). Compound 8 was converted into methyl glycoside (9) by refluxing with methanol and IR 120 resin. 9 was stirred with excess of Raney nickel for 2 days to afford the 6-deoxy product 10 (65%) which was treated with methanesulphonyl chloride-pyridine to give the 3-mesylate 11. Nucleophilic displacement reaction of 11 with sodium azide in dimethylformamide at 100° then yielded the azido-derivative 12. Compound 12 has been converted into L-daunosamine hydrochloride (13) in two steps Via reduction and hydrolysis.[7]



It is pertinent to mention that the procedure reported above is suitable to prepare 2,6-dideoxy-L-sugars which are often encountered in natural products and are prepared by lengthy routes.

The authors thank Dr.A.V.Rama Rao for his keen interest.

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(Received in UK 5 January 1987)