The Synthesis of Daunosamine

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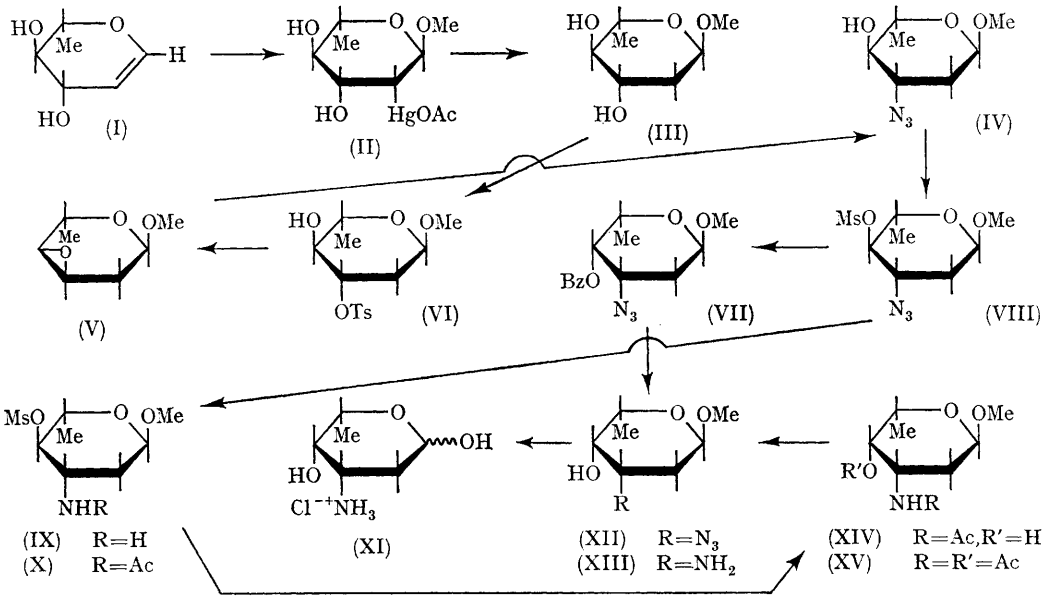
DAUNOMYCIN[1] is a cytotoxic antibiotic whose antitumor activity has been studied.[2] The compound consists of an aglycone, daunomycinone,[3a] and a sugar, daunosamine.[3b] The sugar has been shown to be 3-amino-2,3,6-trideoxy-L-*lyxo*-hexose; synthesis of a derivative of the D-enantiomer has been announced recently.[4] This Communication describes the synthesis of the natural L-sugar isolated as its hydrochloride (XI).

The conversion of L-rhamnose into L-rhamnal (I)

followed the literature procedure.[5] Methoxymercuration to (II), followed by reduction with potassium borohydride[6] furnished the 2,6-dideoxysugar (III) which is the enantiomer of methyl chromoside C.[7] The 3-*O*-monotoluene-*p*-sulphonate (VI), m.p. 86·5—86·9°, $[\alpha]_D$ −116 ($CHCl_3$), was the principal product of the sulphonylation of (III), and could readily be separated by column chromatography as a crystalline solid from the minor amount of ditoluene-*p*-sulphonate that accompanied it. Reaction with methanolic sodium methoxide converted (VI) into the epoxide (V) which, without isolation, was opened with sodium azide to form mainly the 3-azido-sugar, the expected product based on conformational considerations. The crude azide (IV) was converted into the crystalline methanesulphonate (VIII), m.p. 89—90°, $[\alpha]_D$ −127 ($CHCl_3$). Two paths were available for the conversion of (VIII) into daunosamine hydrochloride (XI). In the preferred route the azidosulphonate (VIII) was treated with sodium benzoate in *NN*-dimethylformamide[8] yielding the benzoate (VII) as an analytically pure oil, $[\alpha]_D$ −194 ($CHCl_3$) after chromatography, which was saponified under very mild conditions with dilute sodium hydroxide in aqueous methanol to give the azido-alcohol (XII), an oil. Catalytic hydrogenation of (XII) afforded the crystalline glycoside (XIII), m.p. 109—110°, $[\alpha]_D$ −210 ($CHCl_3$). Alternatively, (VIII) was hydrogenated to the aminosulphonate (IX) which gave a crystalline *N*-acetate (X), m.p. 140—141°, $[\alpha]_D$ −135 ($CHCl_3$). Neighbouring-group displacement of the methanesulphonate in aqueous 2-methoxyethanol containing sodium acetate[9] yielded the *N*-acetate (XIV) and thence the crystalline *NO*-diacetate (XV), m.p. 187—188°, $[\alpha]_D$ − 204 ($CHCl_3$) which had a greater negative rotation than the derivative isolated from daunomycin[3b] but which agreed well in properties with the synthetic derivative in the D-series.[4] Saponification of (XV) gave (XIII), identical with the material obtained in the first route.



The hydrolysis of (XIII) in 0·2N-hydrochloric acid at 90° for 90 min. gave, after careful work-up, the crystalline salt (XI), m.p. 160° (decomp.), $[\alpha]_D^{26}$ −59·4 → −54·2, which was identical chromatographically with an authentic sample.†

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