

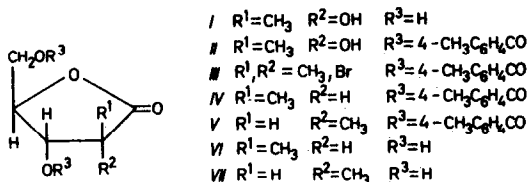
NUCLEOSIDES OF (2R)-2-C-METHYL-2-DEOXY-ERYTHRO-D-PENTOSE

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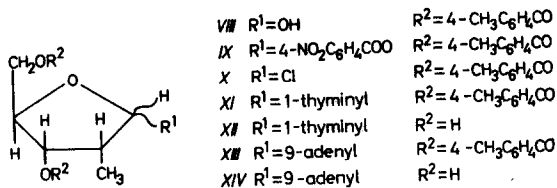
We wish to report the synthesis of some derivatives of hitherto unknown 2-C-methyl-2-deoxy-erythro-D-pentose with the absolute R configuration at C₍₂₎. This sugar can be considered as an isoster of D-ribose. The synthesis proceeds from 2-C-methyl-D-ribonolactone (I), which was partially esterified to compound II. This reacted with HBr to give bromolactone III. Hydrogenolysis of III gave rise to two isomeric protected deoxylactones m.p.122° (IV) and 137° (V). Their configuration was determined on the basis of ORD curves of both free lactones (VI and VII) obtained from IV and V. The isomer VI, originating from IV shows the first Cotton effect extremum at 235 nm positive whereas isomer VII prepared from V has the same extremum negative. Sugar 1,4-lactones with OH-group at C₍₂₎ with an R configuration display negative values of $[\alpha]_{235}$ and vice versa¹. The fact that the optical rotation of 2-C-methyl-D-ribo-1,4-lactone is very low ($[\alpha]_{235} -860, H_2O$)² in comparison with that of the D-ribo-1,4-lactone ($[\alpha]_{235} -5200, H_2O$)² indicates that the rotation parameters of the methyl and hydroxyl group are approximately of the same magnitude. Hence we assume that the configuration of VI and VII are S and R, respectively.



As our chief interest was in compounds with 2R configuration we used for further synthesis the protected lactone melting at 137° (V). We reduced it with diisiamylborane³ and obtained protected pentofuranose VIII, which was con-

verted to p-nitrobenzoylderivative IX. The p-nitrobenzoyloxy group was replaced with chlorine by treatment with HCl and the halogenose formed (X) was allowed to react immediately with 2,4-bis-thimethylsilyloxy-5-methylpyrimidine. From the reaction mixture of anomeric protected nucleosides XI a crystalline compound melting at 203-205° was isolated $[\alpha]_D^{20}$ 18,8°(0.82 CHCl₃). Methanolysis yielded the free (2'R)-1-(2'-C-methyl-2'-deoxy-erythro-1'-D-pentofuranosyl)-thymine XII $[\alpha]_D^{20}$ 25.7°(0.12 H₂O). Mass spectrum: 256 (M), 167 (M-89), 131 (sugar component), 127 and 126 (thymine + 2H, thymine + H)⁴. UV spectrum: λ_{\max} 268 nm, λ_{\min} 234 nm (pH 7); λ_{\max} 267 nm, λ_{\min} 246 nm (pH 12). IR spectrum 1715 cm⁻¹, 1692 cm⁻¹ (CO), 3394 cm⁻¹ (N₍₃₎H).

Halogenose X was treated with chlormercuri-N-benzoyladenine to obtain a mixture of anomeric protected nucleosides XIII from which a crystalline compound was isolated, m.p.119°, $[\alpha]_D^{20}$ -38,5°(0.43 CHCl₃). This was subjected to methanolysis to yield sirupy (2'R)-9-(2'-C-methyl-2'-deoxy-erythro-1'-D-pentofuranosyl)-adenine XIV $[\alpha]_D^{20}$ 5,9°(0.092 H₂O). Mass spectrum: 265 (M), 179 (M-89), 136 and 135 (adenine + 2H, adenine + H), 131 (sugar component)⁴. UV spectrum: λ_{\max} 260 nm, λ_{\min} 228 nm (pH 7); λ_{\max} 260 nm, λ_{\min} 228 nm (pH 12).



Compounds I - V, VIII, IX, XI and XIII are crystalline and their elementary analyses were satisfactory. The configuration of the two nucleosides and the results of biological tests will be reported later.

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