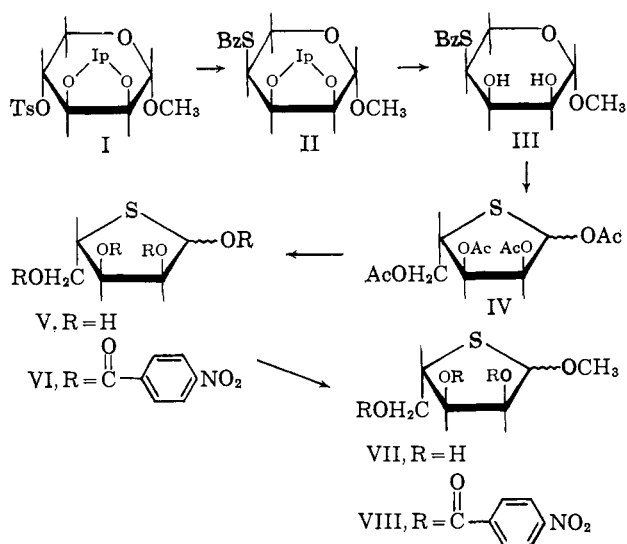


4-Thio-L-ribose: A Thiofuranose Sugar¹

Sir:

There has been a considerable interest in recent years in the synthesis of thio sugars in which the ring oxygen atom has been replaced by sulfur. Thus, 5-thio-D-xylose,² 5-thio-D-ribose,³ and 5-thio-D-glucose⁴ have been synthesized. In all cases the sulfur atom assumed the ring position to give a thiopyranose configuration rather than the isomeric furanose in which the ring closed on oxygen. The biological importance of D-ribofuranose in the nucleic acids prompted us to investigate the synthesis of 4-thio-ribose with the hope that the sulfur atom would again assume the ring position to give a thiofuranose. The synthesis of 4-thio-L-ribofuranose⁵ is the subject of the present communication.

Methyl 2,3-O-isopropylidene-4-O-(*p*-tolylsulfonyl)- α -D-lyxopyranoside (I) was prepared from D-lyxose by es-



entially the same method described by Kent and Ward.⁶

Treatment of I with potassium thiobenzoate in N,N-dimethylformamide (DMF) gave methyl 4-S-benzoyl-2,3-O-isopropylidene-4-thio-L-ribofuranoside (II) as a sirup. Deacetylation of II with aqueous acetic acid yielded crystalline methyl 4-S-benzoyl-4-thio-L-ribofuranoside (III), m.p. 148–149.5°. *Anal.* Found: C, 54.9; H, 5.64; S, 11.3. Acetolysis of III with acetic anhydride and sulfuric acid gave a chromatographically homogeneous analytically pure sirup which showed no thiol ester absorption in the infrared and which must be the thiofuranose tetra-O-acetate⁷ (IV), $[\alpha]^{25}_{\text{D}} +56^{\circ}$ (1.3% in chloroform). *Anal.* Found: C, 46.5; H, 5.22; S, 9.81. Deacetylation of IV with methanolic sodium methoxide gave 4-thio-L-ribofuranose (V) as an analytically pure sirup (*Anal.* Found:

C, 36.2; H, 6.3; S, 19.1) characterized as the tetra-*p*-nitrobenzoate (VI), m.p. 216–217°; $[\alpha]^{25}_{\text{D}} +30^{\circ}$ (1.36% in chloroform). *Anal.* Found: C, 52.0; H, 2.95; N, 7.28; S, 4.16.

Sirupy 4-thio-L-ribose reacted rapidly with aqueous iodine solution at room temperature to about the theoretical uptake for one thiol group, after which there was a relatively slow additional iodine consumption. This contrasts with the behavior of 5-thio-D-xylopyranose^{2b} and 5-thio-D-ribofuranose,³ which reacted only slowly with aqueous iodine solution with intermittent heating.^{2b} Titration of V with silver nitrate⁸ showed one equivalent of thiol. That the sirupy 4-thio-L-ribose exists primarily in the furanose form was decided from spectral evidence. The absence of significant amounts of absorption at 5.75 and 3.90 μ indicative of the carbonyl and free thiol,⁹ respectively, eliminated both the open-chain sugar and the 4-thio-L-ribofuranose as major structural contributors, although small quantities of either would probably not be detected.

Treatment of V with methanolic hydrogen chloride gave the glycoside (VII) as a sirup which was characterized as the crystalline tris-*p*-nitrobenzoate hydrate (VIII), m.p. 107–108.5°, resolidified at 110°, remelted 195–195.5°, $[\alpha]^{24}_{\text{D}} -89^{\circ}$ (1% in chloroform). *Anal.* Found: C, 50.2; H, 3.38; N, 6.04; S, 4.85. A nitroprusside test on the glycoside (VII) was negative, indicating that ring formation was exclusively on sulfur. This was further established by the infrared spectrum of the *p*-nitrobenzoate (VIII) which showed no evidence for a thiol ester.

It is interesting to note that reactions which involved C-1 of 4-thioribose (V) gave thiofuranose products in which the ring closed on sulfur (e.g., IV and VII) rather than the isomeric pyranoses in which the ring must close on oxygen.

(8) B. Saville, *Analyst*, **86**, 29 (1961).

(9) Debenzoylation of III with methanolic sodium methoxide gave methyl 4-thio- β -L-ribofuranoside in which there was thiol absorption at 3.90 μ . Thus the absence of absorption at 3.90 μ in V is indicative of the absence of a free thiol.

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Isomerization of Cyclononatrienes

Sir:

In a recent communication concerning base-catalyzed isomerization of medium ring dienes and trienes, Gardner and co-workers¹ reported the conversion of 1,2,6-cyclononatriene (I) to a mixture of 4,7-dihydroindane (II) and an isomeric bicyclic material, either III or IV, by potassium *t*-butoxide (KOBu) in dimethyl sulfoxide (DMSO) in 2 hr. at 70°. Two intermediates in the isomerization sequence were observed after reaction for 2 hr. at 27°, and these appeared also to be bicyclo-[4.3.0]nonadienes. A sample of 1,3,6-cyclononatriene, obtained from 9,9-dibromo[6.1.0]non-2-ene, was recovered unchanged after being subjected to the isomerizing conditions for 144 hr. at 70°. Thus, it was concluded that 1,3,6-cyclononatriene is not an intermediate in the bridging isomerization I to II. In this communication we report some pertinent observations regarding cyclononatriene isomerizations made while examining *cis-cis-cis*-1,4,7-cyclononatriene² (V) out of curiosity about the nature and behavior of carbanions derived from this hydrocarbon.

As summarized in Table I, in 1.2 M solution in DMSO, 0.7 M in KOBu, 1,4,7-cyclononatriene (V) at

(1) D. Devaprabhakara, C. G. Cardenas, and P. D. Gardner, *J. Am. Chem. Soc.*, **85**, 1553 (1963).

(2) P. Radlick and S. Winstein, *ibid.*, **85**, 344 (1963).

(1) The work reported in this communication was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service, Contract No. SA-43-ph-1892. The opinions expressed in this paper are those of the authors and are not necessarily those of the Cancer Chemotherapy National Service Center.

(2) (a) J. C. P. Schwarz and K. C. Yule, *Proc. Chem. Soc.*, 417 (1961); (b) T. J. Adley and L. N. Owen, *ibid.*, 418 (1961); (c) R. L. Whistler, M. S. Feather, and D. L. Ingles, *J. Am. Chem. Soc.*, **84**, 122 (1962).

(3) C. J. Clayton and N. A. Hughes, *Chem. Ind. (London)*, 1795 (1962).

(4) M. S. Feather and R. L. Whistler, *Tetrahedron Letters*, 667 (1962).

(5) The commercial availability of D-lyxose for a starting material suggested the model synthesis of 4-thio-L-ribose, rather than the biologically significant 4-thio-D-ribose which would require L-lyxose for a starting material.

(6) P. W. Kent and P. F. V. Ward, *J. Chem. Soc.*, 416 (1953).

(7) A similar reaction was described by Feather and Whistler⁴ where the acetolysis of 1,2-O-isopropylidene 3,5,6-O,S,O-triacetyl-5-thio-D-glucopyranose resulted in ring expansion to give 1,2,3,4,6-penta-O-acetyl-5-thio-D-glucopyranose.