Tetrahedron Letters No. 13, pp 1171 - 1172, 1978. Pergamon Press. Printed in Great Britain.

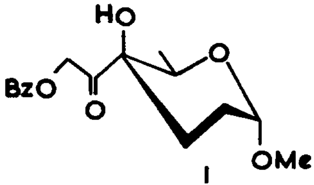
A SYNTHESIS OF A DERIVATIVE OF PILLAROSE

By J.S. Brimacombe*, A.M. Mather, and R. Hanna

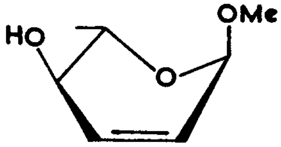
Chemistry Department, University of Dundee, Dundee DD1 4HN

(Received in UK 6 February 1978; accepted for publication 9 February 1978)

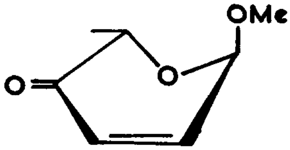
Pillarose is the branched-chain sugar component of pillaromycin A[1], an anthracycline antibiotic elaborated by *Streptomyces flavovirens*. In common with other members of the anthracycline group of antibiotics, pillaromycin A displays antitumour activity. The structure originally assigned[2] to pillarose has been revised to 2,3,6-trideoxy-4-*C*-glycolyl-L-*threo*-hexose in the light of a crystallographic study[3] on pillaromycin A and elegant synthetic work by Fraser-Reid's group[4] that culminated in the synthesis of the benzoate derivative 1 of methyl α-D-pillaroside. A synthesis of the corresponding derivative of L-pillarose was recently reported by Paulsen's group,[5] who used the dianion derived from 2-hydroxymethyl-1,3-dithiane to introduce the branched-chain functionality. In the previous communication we showed that methoxyvinyl-lithium serves as an acyl anion equivalent which allows a variety of branched-chain structures to be derived from the same adduct. A related series of reactions on methyl 2,3,6-trideoxy-α-L-*glycero*-hexopyranosid-4-ulose (4) has provided a convenient synthesis of the crystalline derivative 8 of pillarose.



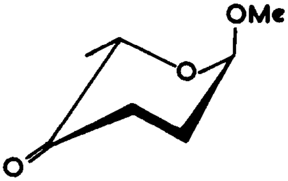
1



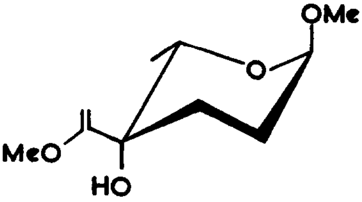
2



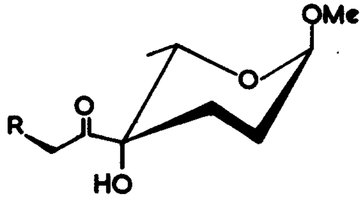
3



4



5



6 R = H
7 R = OH
8 R = OBz

Oxidation of the allylic alcohol 2 (readily obtained[6] from L-rhamnose) with freshly prepared manganese dioxide in chloroform at room temperature gave the enone 3 (86%), m.p. 51-52° (after sublimation at 50° and *ca.* 15 mmHg), $[\alpha]_D$ - 12° (*c* 1, chloroform), which, after hydrogenation over 5% palladised charcoal and chromatography, furnished the keto-sugar **4** (78%), b.p. 80°(bath) at 16 mmHg , $[\alpha]_D$ - 254° (*c* 1.1, chloroform). Catalytic hydrogenation of the allylic alcohol **2** over Adams' catalyst and oxidation of the saturated analogue with ruthenium tetroxide in carbon tetrachloride also gave the keto-sugar **4**, but in lower overall yield. The keto-sugar **4** reacted with methoxyvinyl-lithium[7] in tetrahydrofuran under nitrogen at -65° to give the crude adduct **5** (50%), b.p. 103°(bath) at 0.5 mmHg, $[\alpha]_D$ - 92 ± 3° (*c* 1, chloroform), which was used in subsequent reactions without further purification, since attempts to remove impurities by column chromatography on silica gel led to its hydrolysis to the *C*-acetyl derivative **6**, b.p. 120°(bath) at 0.8 mmHg, $[\alpha]_D$ - 96° (*c* 1, chloroform). Hydrolysis of the adduct **5** with 0.02*M* hydrochloric acid in aqueous *p*-dioxan also gave **6** in excellent yield. ^{1}H N.m.r. spectroscopy indicated that the crude adduct **5** is predominantly a single diastereoisomer, whose structure follows from its subsequent conversion into the benzoate **8**.[5] Thus, oxidation of **5** with a molar equivalent of *m*-chloroperbenzoic acid in wet ether at 0-6° for 2h and chromatography on silica gel gave syrupy methyl α-pillaroside **7** (65%), which was benzoylated to give **8**, m.p. 107-108° (from ether-hexane), $[\alpha]_D$ - 93° (*c* 1.3, chloroform). The physical data and ^{1}H n.m.r. spectrum of **8** are in accord with those of the corresponding derivative of natural pillarose.[2]

New compounds had elemental analyses and/or spectroscopic properties compatible with the structures assigned.

References

[1] M. Shibata, M. Asai, K. Mizuno, A. Miyake, and S. Tatsuoka, *Proc.Jap.Acad.*, 1964, **40**, 296; M. Asai, *Chem. and Pharm.Bull.(Japan)*, 1970, **18**, 1699, 1706; M. Asai, E. Mizuta, K. Mizuno, A. Mikaye, and S. Tatsuoka, *ibid.*, 1970, **18**, 1720.

[2] M. Asai, *Chem. and Pharm.Bull.(Japan)*, 1970, **18**, 1713.

[3] J.O. Pezzanite, J. Clardy, P.-Y. Lau, G. Wood, D.L. Walker, and B. Fraser-Reid, *J.Amer.Chem. Soc.*, 1975, **97**, 6250.

[4] D.L. Walker and B. Fraser-Reid, *J.Amer.Chem.Soc.*, 1975, **97**, 6251.

[5] H. Paulsen, K. Roden, V. Sinnwell, and W. Koebernick, *Angew.Chem.Internat.Edn.*, 1976, **15**, 439.

[6] J.S. Brimacombe, L.W. Doner, and A.J. Rollins, *J.C.S. Perkin I*, 1972, 2977.

[7] J.E. Baldwin, G.A. Höfle, and O.W. Lever, jun., *J.Amer.Chem.Soc.*, 1974, **96**, 7125.