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SYNTHESIS OF N-BENZOYL-L-RISTOSAMINE

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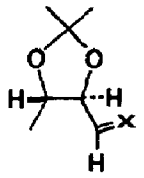
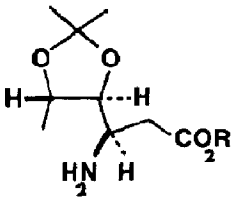
The synthesis of N-benzoyl-L-ristosamine (7) from natural tartaric acid through the intermediacy of the δ-xylo and γ-ribo lactones (4) and (6) is reported

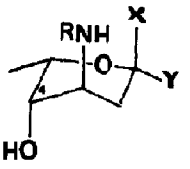
We reported obtaining from the C_4 chiral compound (1) and from its enantiomer, prepared from natural tartaric acid and from L-threonine (or the unnatural form of tartaric acid), respectively, the N-benzoyl derivate of 3-epi-L-daunosamine (2,3,6-trideoxy-3-amino-L-xylo-hexose) (5) and its D-enantiomer.[1] Key intermediates in the synthesis were the C_6 α,β-unsaturated ester (2), the β-amino ester (3) and the δ-lactone (4). The D-enantiomer of the xylo lactone (4) has been converted into the L-arabino and L-lyxo configurational isomers. From these compounds the N-trifluoroacetyl derivates of L-acosamine and L-daunosamine have been prepared.[2]



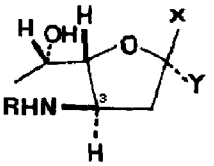
(1) X=O
(2) X= $CHCO_2Et$



(3) R=Et



(4) R=COC_6H_5; X,Y=O
(5) R=COC_6H_5; X,Y=H,OH



(6) R= COC_6H_5; X,Y=O
(7) R= COC_6H_5; a: X=OH; Y=H
b: X=H; Y=OH

Now we refer to the synthesis of the N-benzoyl derivate of L-ristosamine (7), the amino deoxy sugar component of the antibiotic ristomycin,[3] with the L-ribo configuration, from (1) through the key intermediacy of the L-xylo-δ-lactone (4). In this way, from natural and unnatural tartaric acid, the L- and D-enantiomeric forms of the four configurational isomers of 2,3,6-trideoxy-3-amino-hexose can be formally prepared, thus increasing the significance of C_4 chiral intermediates to the synthesis of the optically active forms of natural products.[2,4]

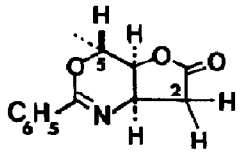
Thus, the δ-lactone (4) was converted into the 4-O-mesyl derivate under standard conditions in 80% yield. The mesylate , upon boiling with aqueous sodium acetate gave rise, in ~75% yield, to the γ-lactone (6), m.p. 149°, $[\alpha]_D^{20}$ +37° (C 0.95,EtOH). Its structure rests on ^{1}H-n.m.r. studies (Table) and comparison of these data with those of the other configurationally isomeric γ-lactones.[1,2] Compound (6) upon DIBAH reduction in THF at -40°C yielded (65%) N-benzoyl-L-ristosamine (7), m.p. 130-132°C, $[\alpha]_D^{20}$ -12° (10 min)(c 1,EtOH), well in agreement with the

literature values.[3] The ^{1}H-n.m.r. spectrum of (7) requires some comments. Soon after the solution in DMSO, the β-anomer (7a) represents ca. 60% of the α-β mixture. Within one day the equilibrium value of ca. 50% is reached. The stereochemical assignement of the two anomers is made on the basis of the upfield shift undergone by the protons syn to a vicinal substituent in a pentacyclic system.[5] In the β-anomer (7a) the H-2 proton 'sees' at its side two vicinal substituents, and the chemical shift difference between H-2 and H-2' is 0.61 ppm. The H-2 and H-2' in the α-anomer (7b) have only one syn vicinal substituent: with respect to the β-anomer H-2 and H-2' go downfield and upfield, respectively, showing exactly the same chemical shift. Apart from the substituent influence on vicinal protons, it is known[5] that a substituent exerts a deshielding effect on the cis-γ-protons in the 5-membered rings. We can observe that going from the β to the α anomer H-3 is deshielded by 0.24 ppm and H-4 is shielded by about 0.21 ppm; this observation strongly supports a trans relationship between H-3 and H-4.

TABLE: ^{1}H-n.m.r. data*

	(6)			(7a)			(7b)		
H-1				5.43	J(1,2)	2.1	5.42	J(1,2)+ J(1,2')	7.2
H-2	2.54	J(2,2')	18.3	1.69	J(1,2')	4.9	2.06†	J(2,3)+ J(2',3)	16.0
H-2'	2.96	J(2,3)	4.0	2.30	J(2,2')	13.2	2.06†		
H-3	4.73	J(2',3)	9.3	4.44	J(2,3)	4.5	4.68		
H-4	4.34	J(3,4)	3.1	3.91	J(2',3)	8.8	~ 3.70Δ		
H-5	3.91	J(4,5)	3.1	~ 3.70Δ	J(3,4)	4.8	~ 3.70Δ		
CH_3	1.17	J(5,6)	6.6	1.07	J(4,5)	4.8	1.10		
OH-1				6.32	J(5,6)	6.4	6.32	J(5,6)	6.0
OH-5	5.14	J(5,OH)	4.5	4.63	J(1,OH)	5.3	4.54	J(1,OH)	5.3
NH	8.97	J(3,NH)	7.5	8.37	J(5,OH)	4.5	8.55	J(5,OH)	3.0
					J(3,NH)	7.6		J(3,NH)	8.0

* Solvent: $(CD_3)_2SO$; chemical shifts in ppm from int. TMS; J in Hz
† Since H-2 and H-2' of (7b) have the same chemical shift, H-1, H-2, H-2' and H-3, H H-2' are deceptively simple ABX systems, and only the value J(AX)+ J(BX) can be gi
Δ Partially overlapped signals



(8)

Under the conditions in which the 5-O-mesyl derivate of the γ-xylo N-benzoyl lactone isomer of (4) gave (8), $[\alpha]_D^{20}$ -4.4° (c 1, EtOH), the 4-O-mesylate of (4) gave (6) as sole react product. The ^{1}H-n.m.r. data of (8) are (DMSO-d_6): δ 2.47 (J(17);3.18 (J(2,3) 1.8); 4.21 (J(2',3) 7.3); 4.57 (J(3,4) 4.5); 4.47 (J(4,5) 2.7); 1.35 (J(5,6) 6

[1] G.Fronza, C.Fuganti, P.Grasselli, G.Marinoni, Tetrahedron Letters,1979,3 88
[2] G.Fronza, C.Fuganti, P.Grasselli, J.Chem.Soc.Chem.Comm.1980, in press [3] R.Bognar, F .Sztaricska M.E.Munk, J.Tamas, J.Org.Chem., 1974,2971 [4] E.Hungerbühler, D.Seebach, D.Wasmuth, Angew.Chem (Int.Eng.Ed.),1979, 958 [5] M.Anteunis, D.Danneels, Org.Magn.Res., 1975,3 45

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