Structure and Conformation of *N*-Benzoyl Derivatives of the Biologically Important 3-Amino-2,3,6-trideoxy-L-hexoses and their Synthetic Precursor γ- and δ-Lactones; a ^{1}H and ^{13}C Nuclear Magnetic Resonance Study

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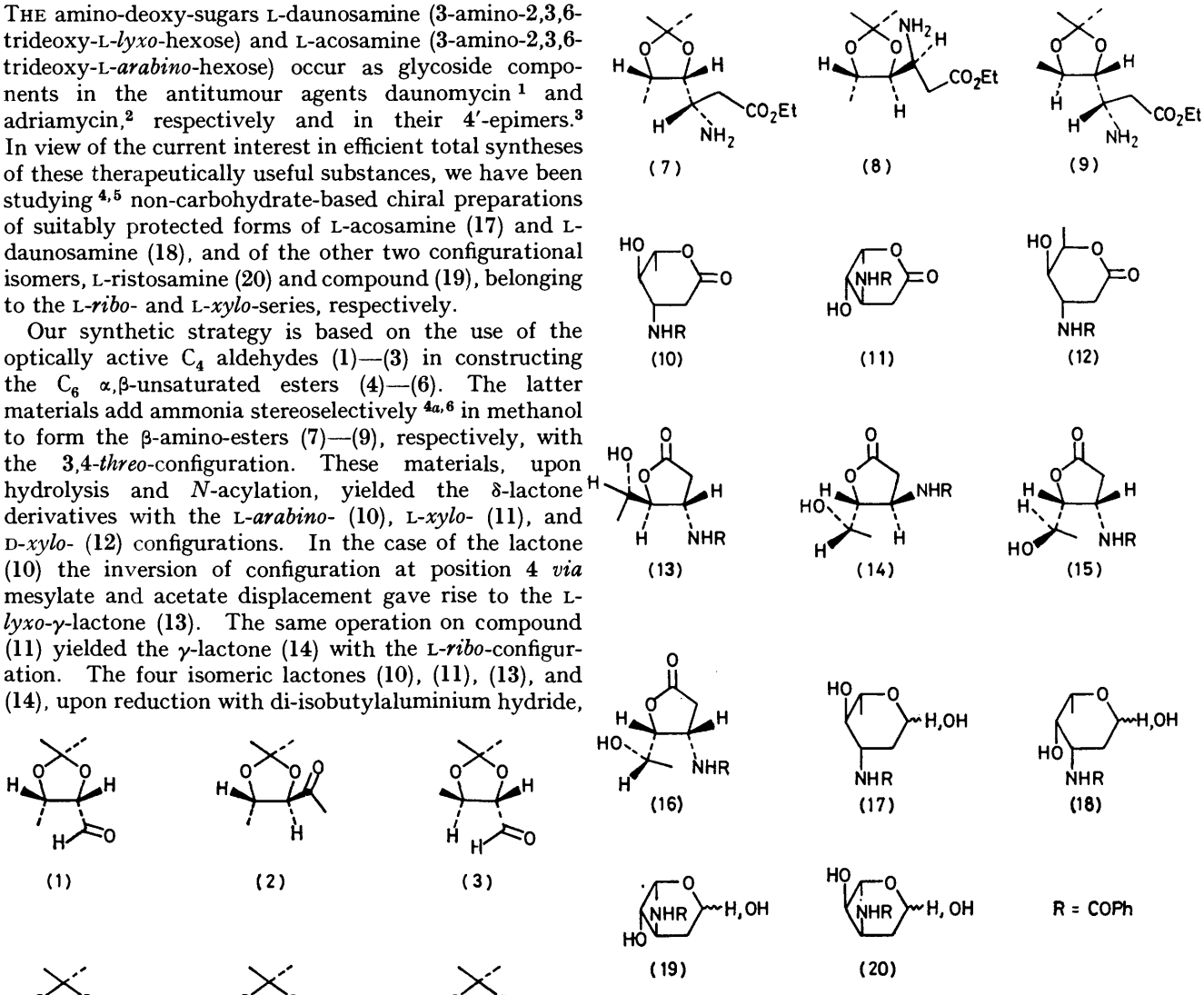
The 3-benzoylamino-2,3,6-trideoxy-L-*xylo*- and L-*arabino*-hexoses have been shown to exist in the α- and β-pyranose forms, whereas the compounds with the L-*ribo*- and L-*lyxo*-configurations exist as mixtures of α- and β-pyranose and α- and β-furanose tautomers. All the pyranoid compounds are stable in the $^1C_4$ (L) conformation except the L-*xylo*-α-derivative, which exists in a conformational equilibrium with about 15% of the $^4C_1$ (L) form. The L-*ribo*-α- and β-furanoses adopt the $^1T_2$ (or E_2) and $^2T_1$ (or ^2E) conformation, respectively. The γ-lactones exist in a conformational equilibrium except the L-*arabino*-γ-lactone, which exists in the $^4T_3$ (or E_3) conformation. The δ-lactones preferentially adopt the half-chair conformation although some distortions must be invoked for the L-*arabino*-δ-lactone to account for the observed coupling constants.

THE amino-deoxy-sugars L-daunosamine (3-amino-2,3,6-trideoxy-L-*lyxo*-hexose) and L-acosamine (3-amino-2,3,6-trideoxy-L-*arabino*-hexose) occur as glycoside components in the antitumour agents daunomycin [1] and adriamycin,[2] respectively and in their 4'-epimers.[3] In view of the current interest in efficient total syntheses of these therapeutically useful substances, we have been studying [4,5] non-carbohydrate-based chiral preparations of suitably protected forms of L-acosamine (17) and L-daunosamine (18), and of the other two configurational isomers, L-ristosamine (20) and compound (19), belonging to the L-*ribo*- and L-*xylo*-series, respectively.

Our synthetic strategy is based on the use of the optically active C_4 aldehydes (1)—(3) in constructing the C_6 α,β-unsaturated esters (4)—(6). The latter materials add ammonia stereoselectively [4a,6] in methanol to form the β-amino-esters (7)—(9), respectively, with the 3,4-*threo*-configuration. These materials, upon hydrolysis and *N*-acylation, yielded the δ-lactone derivatives with the L-*arabino*- (10), L-*xylo*- (11), and D-*xylo*- (12) configurations. In the case of the lactone (10) the inversion of configuration at position 4 *via* mesylate and acetate displacement gave rise to the L-*lyxo*-γ-lactone (13). The same operation on compound (11) yielded the γ-lactone (14) with the L-*ribo*-configuration. The four isomeric lactones (10), (11), (13), and (14), upon reduction with di-isobutylaluminium hydride, afforded the required amino-sugar derivatives (17), (19), (18), and (20), respectively. Also the lactone (12), belonging to the D-series, served as precursor of L-acosamine (17) and, eventually, of L-daunosamine (18).

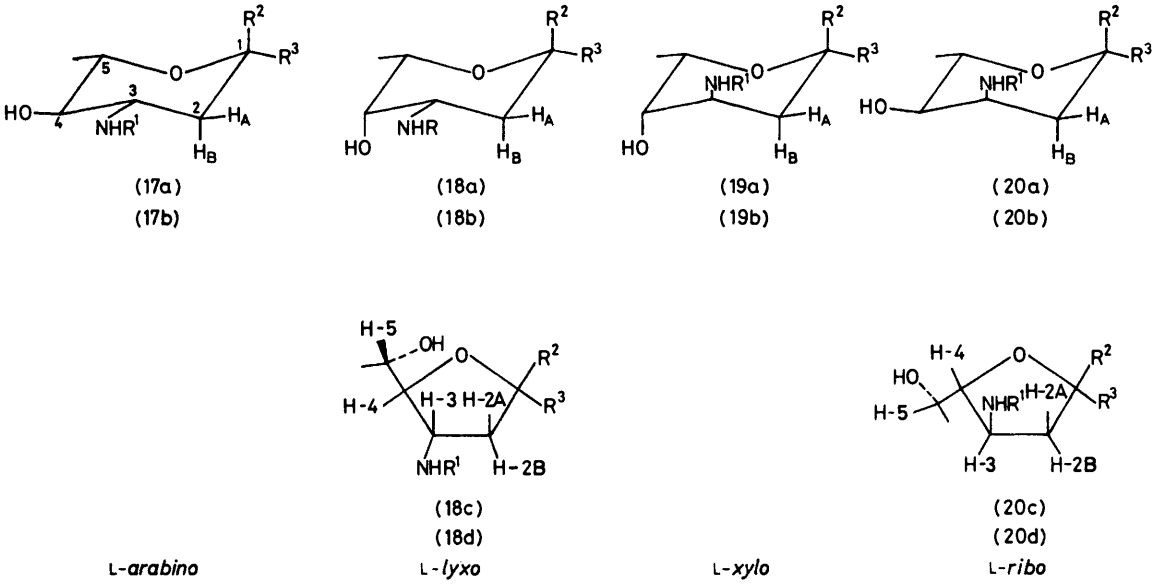


In fact, upon treatment with acid, compound (12) was isomerized to the γ-lactone (15), which by inversion of configuration at position 5, as above, yielded the γ-lactone (16) belonging to the L-*arabino*-series. Compound (16) was converted, upon reduction, into the expected amino-sugar derivative (17).

In the present paper we report the details of n.m.r. studies on the final products (17)—(20) and on the key intermediate lactones (10)—(16), which proved relevant for the synthetic work.

3-*Benzoylamino*-2,3,6-*trideoxy*-L-*hexoses*.—The structural and configurational isomers of the 3-benzoylamino-2,3,6-trideoxy-L-hexoses are shown in Scheme 1. All ring tautomers were detected for the L-*xylo*-hexose). Thus only compounds with a *trans*-arrangement of the substituents at C-3 and C-4 display in solution a certain amount of the furanose structure [74% for the L-*ribo*- (20c, d) and 16% for the L-*lyxo*- (18c, d) derivatives]. With a *cis*-arrangement of substituents the five-membered ring form is destabilized by steric interactions between them.[11] In fact the L-*arabino*- (17a,b) and L-*xylo*- (19a,b) derivatives are stable in the pyranose structure.

The coupling constants ^3J(H-4,OH-4) and ^3J(H-5,-OH-5) were used to distinguish between the six- and five-membered ring structures. First we will discuss the

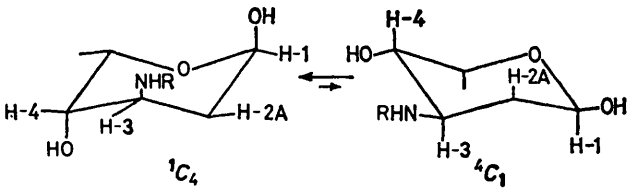


SCHEME 1 R^1 = COPh; designations a and c indicate the α-anomers (R^2 = OH, R^3 = H) and b and d the β-anomers (R^2 = H, R^3 = OH)

these compounds had been previously isolated or synthesized, and the ^{1}H n.m.r. spectra of a variety of derivatives had been obtained (mainly methyl 3-*N*-acetyl-4-*O*-acetyl-α-pyranosides).[1,4a,6-10] We report here the analysis of ^{1}H and ^{13}C spectra of the *N*-benzoyl derivatives of the above amino-sugars, which can exist in solution as α- and β-anomers of six- and five-membered ring structures. In particular we found that, just after dissolution in dimethyl sulphoxide, compounds with L-*arabino*- (17), L-*lyxo*- (18), and L-*xylo* (19) configurations exist as α-pyranoses (100%), whereas the L-*ribo*-derivative (20) exists as a mixture of α- (57%) and β- (43%) furanose tautomers. During *ca.* 1 week, both the L-*lyxo*- and L-*ribo*-compounds isomerized slowly to afford a mixture of α- and β-pyranose and α- and β-furanose forms (see Table 4 for the relative amounts of the tautomers). In contrast the L-*xylo*- and L-*arabino*-compounds after 1 week still existed as α- and β-anomers of the six-membered ring form (only traces of the five-membered proton spectra of pyranoses and furanoses; data for only the more abundant isomers of the tautomeric mixtures are reported in Tables 1 and 2, namely the L-*arabino*- (17a,b), the L-*lyxo*- (18a,b), and the L-*xylo*- (19a,b) pyranoses, and the L-*ribo*- (20c,d) furanoses. Then the ^{13}C spectra will be discussed together with those of the γ- and δ-lactones.

Pyranoses (17a,b)—(19a,b). The α- and β-anomers were distinguished by the value of ^3J(1,2B) which changes from *ca.* 3.5 Hz for the α- to *ca.* 9.5 Hz for the β-anomer. The signals of the methylene protons H-2A and H-2B were assigned from the values of ^3J(1,2) and ^3J(2,3) for all isomers except for (19a), because the latter does not display any diaxial coupling constant. Bognar *et al.*[8] and Dyong *et al.*[9] have reported the n.m.r. spectra of the methyl 3-*N*-acetyl-4-*O*-acetyl-2,3,6-trideoxy-L-*ribo*- and -D-*xylo*-α-pyranosides, respectively. They assigned the C-2 proton signals on the basis of the smaller value of the vicinal equatorial–equatorial coup-

ling than of the axial–equatorial one. In fact they found J(1,2A) *ca.* 1 Hz and J(1,2B) *ca.* 4 Hz. However the difference between these couplings is sometimes, as in our case, too small to allow a safe attribution. Thus the assignment for (19a) was based on the long-range coupling involving the anomeric and hydroxy-protons. The α-anomers (17a) and (18a) display a four-bond coupling constant of *ca.* 1.5 Hz between H-2B and OH-1, whereas H-2A shows no interaction with the hydroxy-proton. Clearly the OH group adopts a preferred conformation, favouring the planar W arrangement H(2B)–C(2)–C(1)–O–H, which is the best pathway for a four-bond interaction. This observation allows an independent and unequivocal assignment of H-2A and H-2B



SCHEME 2

be applied, yielding approximately 85% of the $^1C_4$(L) and 15% of the $^4C_1$(L) form. We note that the methyl 3-*N*-acetyl-4-*O*-acetyl-2,3,6-trideoxy-α-D-*xylo*-pyranoside [a derivative of the enantiomeric form of (19a)] studied by Dyong *et al.*[9] is stable in $CDCl_3$ in the pure $^4C_1$(D) conformation, which is equivalent to the $^1C_4$(L)

TABLE 1

^{1}H Chemical shifts of 3-benzoylamino-2,3,6-trideoxy-L-hexoses [a]

Compd.	H-1	H-2A	H-2B	H-3	H-4	H-5	H-6	OH-1	OH-4	NH	OH-5
(17a)	5.10	1.84	1.66	4.25	3.11	3.81	1.15	6.15	4.85	8.10	
(17b)	4.71	1.94	1.51	3.94	3.08	3.28	1.20	6.51	4.85	8.23	
(18a)	5.17	1.48	2.02	4.41	3.53	4.06	1.11	6.10	4.76	7.95	
(18b)	4.69	1.63	1.79	4.06	3.46	3.56	1.17	6.51	4.75	8.02	
(19a)	5.18	1.50	2.12	4.11	3.37	4.19	1.08	6.73	5.03	8.27	
(19b)	5.02	1.64	1.84	4.11	3.30	3.84	1.12	6.37	4.85	8.18	
(20c)	5.43	1.79	2.30	4.44	3.91	3.65	1.07	6.32		8.37	4.63
(20d)	5.42	2.06	2.06	4.68	3.70	3.70	1.10	6.32		8.55	4.54
(20c) [b]	5.99	2.31	2.62	5.31	4.55	4.25	1.58			8.95	
(20d) [b]	5.94	2.49	2.73	5.66	4.36	4.44	1.61			9.40	

[a] Chemical shifts in p.p.m. from internal Me_4Si; solvent $(CD_3)_2SO$. [b] Solvent C_5D_5N.

TABLE 2

^{1}H Coupling constants of 3-benzoylamino-2,3,6-trideoxy-L-hexoses [a]

Compd.	J(1,2A)	J(1,2B)	J(2A,2B)	J(3,2A)	J(3,2B)	J(3,4)	J(4,5)	J(5,6)	J(1,OH)	J(4,OH)	J(3,NH)	J(2B, OH-1)
(17a)	1.2	3.3	12.5	4.7	12.5	9.4	9.4	6.1	3.7	6.4	8.4	1.6
(17b)	1.9	9.5	12.5	4.6	12.5	9.2	9.5	6.0	6.3	6.2	8.0	
(18a)	1.0	3.4	12.5	4.5	12.5	*ca.* 2	1.0	6.5	3.7	5.7	8.0	1.5
(18b)	2.3	9.4	12.5	4.5	12.5	2.8	1.0	6.5	6.5	5.7	7.5	
(19a)	2.5	4.0	13.5	3.9	4.0	4.4	2.0	6.5	3.6	5.1	7.6	1.3
(19b)	2.1	9.7	13.4	2.5	4.6	3.0	1.5	6.4	6.2	5.5	6.5	
(20c)	2.4	5.0	13.2	4.8	8.9	5.2	4.5	6.4	5.3	4.5 [c]	7.6	
(20d)	7.2 [b]				16.0 [b]			6.0	5.3	3.0 [c]	8.0	
(20c) [d]	*ca.* 1	4.8	13.3	2.5	8.8	4.5	5.0	6.3			6.0	
(20d) [d]	5.3	1.7	12.8	8.0	8.0	5.2	5.2	6.2			8.0	

[a] Coupling constants in Hz; solvent $(CD_3)_2SO$. [b] H-1, H-2A, H-2B and H-3, H-2A, H-2B signals are deceptively simple ABX systems; only the value of J(AX) + J(BX) can be given. [c] J(5,OH). [d] Solvent C_5D_5N.

signals for the isomer (19a), which shows ^4J(OH-1, H-2B) 1.3 Hz.

Inspection of the vicinal coupling constants (Table 2) shows that all the pyranoid compounds are stable in the $^1C_4$(L) conformation [12] (Scheme 2), except for (19a) which displays some deviations in the ^3J values. In particular the equatorial–equatorial couplings J(3,2A) and J(3,4) of (19a) are 1.4 Hz greater than those of (19b), and J(1,2A) is *ca.* 1.5 Hz larger than those of the other anomers (17a) and (18a). These variations can be explained by assuming that the pyranose ring (19a) exists in a conformational equilibrium $^1C_4$(L) ⇄ $^4C_1$(L) (Scheme 2).

In order to estimate the populations P(I) and P(II) of each conformer for (19a), the well known [12] time-average equation J(av) = P(I)J(I) + P(II)J(II) can

conformation. This suggests that the 1,3-*syn*-diaxial interaction between OH-1 and 3-NHR groups is not sufficient to explain the lack of conformational purity in (19a); probably solute–solvent interactions are as important as steric interactions in destabilizing the otherwise preferred $^1C_4$(L) conformation.

Furanoses (20c) *and* (20d). The α- and β-anomers (20c) and (20d) of 3-benzoylamino-2,3,6-trideoxy-L-*ribo*-furanose were distinguished on the basis of the chemical shifts of the ring protons. It is known that the chemical shifts of the ring protons in isomeric five-membered ring systems depend on two general effects: [13] (i) the 1,3- (or γ-) effect, *i.e.* a signal is shifted downfield when a γ-substituent changes from the *anti*- to the *syn*-position, and (ii) the 1,2- (or β-) effect, *i.e.* a signal is shifted upfield when a vicinal substituent changes from the

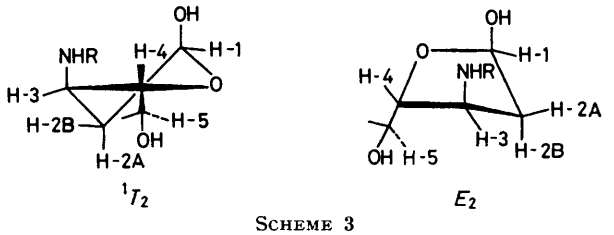
anti- to the *syn*-position. These effects have been investigated [13] mainly with the methyl and acetoxy-substituents and they range in magnitude from about 0.1 to 0.5 p.p.m.

In accordance with the γ-effect due to OH-1, the signals of the ring protons H-3 and H-4 of (20c) are shifted downfield by *ca.* 0.3 p.p.m. and upfield by *ca.* 0.2 p.p.m. with respect to (20d) in both Me_2SO and pyridine as solvents. Furthermore the β-effect induced by OH-1 on the methylene protons allows the attribution of H-2A and H-2B signals in Me_2SO * [H-2A deshielded by 0.27 p.p.m. and H-2B shielded by 0.24 p.p.m. in (20d) with respect to (20c)], whereas in pyridine this effect does not follow the predicted trend (Table 1). The attribution of the methylene proton signals in pyridine was made on the basis of the vicinal coupling constants $^2J(1,2)$. The signals at 2.31 p.p.m. for (20c) and at 2.73 p.p.m. for (20d) display small values of $^3J(1,2)$ (*ca.* 1 and 1.7 Hz, respectively), which are typical for vicinal hydrogens in a *trans*-relationship with torsion angles in the range 80—100°.[14,15] Thus the 2.31 and 2.73 p.p.m. signals are assigned to H-2A of (20c) and H-2B of (20d), respectively.

The values of the vicinal coupling constants suggest that the anomers (20c) and (20d) have different conformations in pyridine. By analogy with the cyclopentane ring,[16] a tetrahydrofuran ring has ten possible envelope (*E*) and ten possible twist (*T*) conformations, which undergo a rapid mutual exchange in the so-called pseudorotational cycle.[15] The value of 4.5 Hz for $^3J(3,4)$ in (20c) corresponds to a torsion angle of 140—150° between H-3 and H-4, and the small values of *ca.* 1 and 2.5 Hz for $^3J(1,2A)$ and $^3J(3,2A)$ can be associated with torsion angles of 80—100°,† indicating that both the substituents at C-1 and C-3 have a pseudoaxial orientation. Therefore the preferred conformation of the α-anomer (20c) is $^1T_2$ or E_2 or a dynamic equilibrium between them (Scheme 3).

In the β-anomer (20d) the coupling constants $^3J(1,2B)$ of 1.7 Hz and $^3J(3,2A)$ of 8.0 Hz correspond to torsion angles of 80—100° (OH-1 quasiaxial) and 170—180° (NHR quasiequatorial), respectively. The value of 5.2 Hz for $^3J(3,4)$ indicates an angle of 140—150° between H-3 and H-4 here too. Consequently the preferred conformation of (20d) is opposite to that of (20c), *i.e.* $^2T_1$ or ^2E or an equilibrium between them.

A phenomenon of some importance in determining the conformation of sugar derivatives is the so-called ' anomeric effect ',[11,17b] resulting from the interaction of



SCHEME 3

the dipoles operating in the two C(1)–O bonds which tend to become oriented in opposite directions, thus stabilizing the pseudoaxial orientation of the OH-1 group. In addition an intramolecular hydrogen bonding between OH-1 and the amide carbonyl may contribute to stabilize the conformation with two 1,3-pseudoaxial substituents for the α-anomer (20c). This conformation is usually less favoured than that with pseudoequatorial groups.[11] In fact the coupling constants $^3J(1,2A)$ and $^3J(3,2A)$ of (20c) increase by 1.4 and 2.3 Hz in Me_2SO with respect to pyridine, corresponding to an increase of the dihedral angles. In this solvent probably the breaking-off of the intra-molecular hydrogen bonding occurs, favouring either a flattening of the ring or a dynamic equilibrium between conformers with ' axially ' and ' equatorially ' oriented groups.

3-Benzoylamino-2,3,6-trideoxyhexono-δ- and -γ-lactones.—δ-Lactones. As shown in Scheme 4, only two of the four possible isomeric δ-lactones were isolated, *i.e.* the L-*arabino*- (10) and the L-*xylo*- (11) derivatives. The ^1H chemical shifts and coupling constants are given in Table 3. There is general agreement that the C–O–CO–C fragment is planar in δ-lactones; [18] the coplanarity of the lactone grouping is attained both in the half-chair and in the boat conformation, whereas it is not allowed in the chair conformation. Early studies on the basis of *X*-ray analysis [19] and o.r.d. data [20] concluded that the boat conformation is preferred for the lactone ring; however i.r.[21] and n.m.r.[22,23] data for some substituted δ-lactones are more consistent with the half-chair conformation. The values of 4.8 and 7.1 Hz for $^3J(2,3)$

TABLE 3

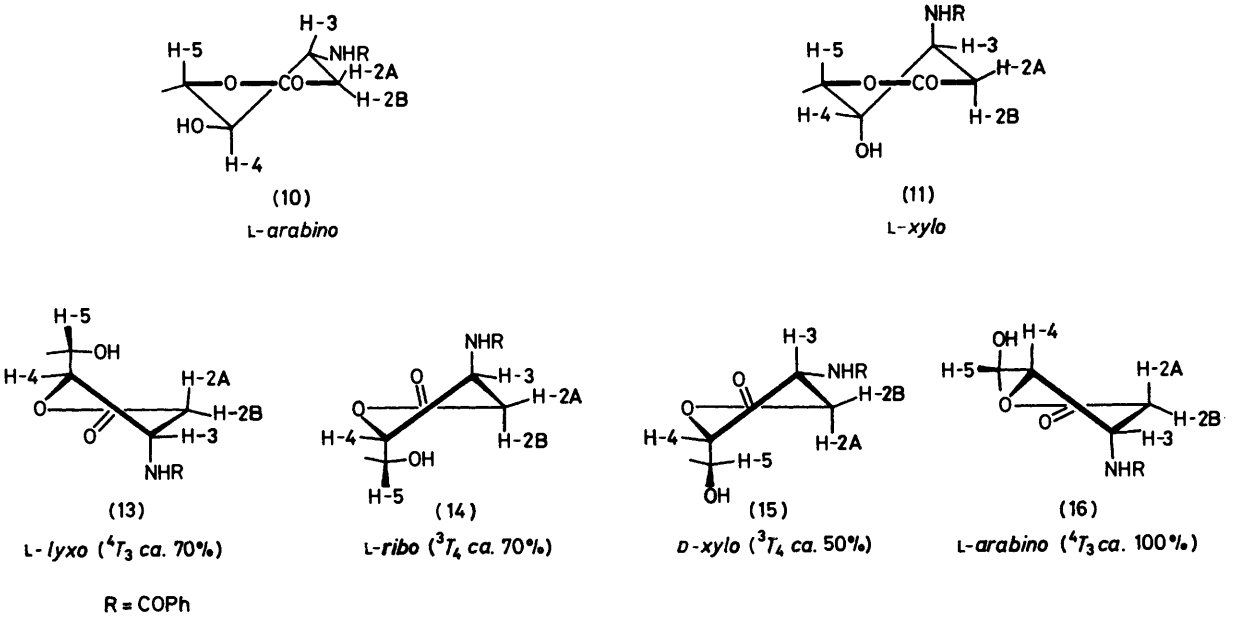
^1H Chemical shifts and coupling constants [a] of 3-benzoylamino-2,3,6-trideoxyhexono-δ- [b] and γ- [c] lactones

Compd.	H-2A	H-2B	H-3	H-4	H-5	H-6	OH	NH	J(2A,2B)	J(2A,3)	J(2B,3)	J(3,4)	J(4,5)	J(5,6)	J(4,OH)
(10)	3.17	2.67	4.44	3.71	4.34	1.42	4.97	8.11	17.3	7.5	7.7	8.4	9.2	6.2	4.8
(11)	2.65	3.03	4.42	3.97	4.77	1.37	4.75	8.09	17.9	4.8	7.1	3.6	1.8	6.5	4.5
(13)	3.16	2.58	4.82	4.37	4.15	1.33	2.31	6.88	18.1	8.9	4.4	3.0	3.0	6.0	
(14)	2.61	3.14	4.85	4.30	4.05	1.37	2.84	6.82	18.2	4.7	9.0	3.6	4.9	6.0	
(15)	2.71	2.94	5.21	4.57	4.15	1.43	2.35	7.68	18.0	6.7	8.7	7.7	3.0	6.5	
(16)	3.07	2.73	5.00	4.32	4.14	1.34	3.96	7.94	18.0	6.6	1.8	4.4	6.4	6.3	

[a] Chemical shifts in p.p.m. from internal Me_4Si; coupling constants in Hz. [b] Solvent $(CD_3)_2CO$. [c] Solvent $CDCl_3$.

* Some overlapped signals occur in the spectrum of (20d) in Me_2SO (Table 1), and several coupling constants cannot be given (Table 2).

† It is well known that $^3J(H,H)$ decreases with increase in the electronegativity of the substituents; [17a] since C-1 is linked to two oxygen atoms $^3J(1,2A)$ is expected to be *ca.* 1.5 Hz smaller [17b] than $^3J(3,2A)$, although the torsion angles between H-1 and H-2 and between H-2 and H-3 are nearly the same.



SCHEME 4

for the L-*xylo*-δ-lactone (11) immediately rule out the boat conformation $^{2,5}B$, since in that case a coupling constant of 10—12 Hz between H-2A and H-3 would be expected. Moreover, according to Barfield and Grant,[24] the geminal coupling constant J(2A,2B) is dependent upon the torsion angle between the CH and CO bonds, reaching a maximum value when the carbonyl group bisects the H–C–H angle. Äyräs and Pihlaja,[25] in a conformational study of several substituted 4-oxo-1,3-dioxans, found values of 17.8 and 15.3 Hz for J_{gem} in compounds with a half-chair and a boat conformation, respectively. The value of 17.9 Hz for ^2J(2A,2B) in (11) strongly supports the half-chair $^3H_4$ conformation for this compound. In this structure the OH and NHR substituents are axially oriented and they induce on H-2B and H-5 a strong deshielding relative to the lactone (10) due to the 1,3-*syn*-diaxial interactions.[26] This observation confirms the preferred half-chair conformation for (11) and allows the assignment of the methylene proton signals in (10) and (11).

The value of 17.3 Hz for ^2J(2A,2B) in the L-*arabino*-δ-lactone (10) is also in agreement with a half-chair conformation. On the other hand the ^3J(2B,3) value of 7.7 Hz is better accommodated by a flattened half-chair where C-3 atom is closer to the C–O–CO–C plane than by a half-chair conformation (see Scheme 4), since in the latter we should expect a ^3J(3,2B) value of 10—12 Hz for the *trans*-diaxial H-3 and H-2B. A similar conformation has been proposed by Sheppard and Turner [22] to explain the n.m.r. data of some steroidal lactones.

γ-Lactones. All the γ-lactone derivatives are reported in Scheme 4, and the ^{1}H chemical shifts and coupling constants are collected in Table 3. The signals of the methylene protons H-2A and H-2B can be assigned on the basis of the γ- and β-effects of the substituents on the ring protons. For instance, in going from (13) to (16) and from (15) to (14), the H-2A signal is shifted upfield and that of H-2B downfield by 0.1—0.2 p.p.m., owing to the γ-effect of the CHOHMe group.[13] Also the β-effect is consistent with that predicted by Anteunis *et al.*,[13] ranging from 0.2 to 0.46 p.p.m., except for H-4, which is shielded only by 0.02 p.p.m. in (14) with respect to (16).

The vicinal coupling constants for γ-lactones have been studied extensively by several authors [27-30] and can be divided into three groups: (i) ^3J 5—9 Hz for *cis* hydrogens, (ii) ^3J 10—12 Hz for *trans*-pseudoaxial hydrogens, and (iii) ^3J 0—1.5 Hz for *trans*-pseudoequatorial hydrogens. As the L-*arabino*-γ-lactone (16) exhibits a small coupling (1.8 Hz) between the two *trans*-protons H-2B and H-3, the preferred conformation for (16) is $^4T_3$ or E_3 (or an equilibrium between them), with a pseudoaxial and a pseudoequatorial orientation of the two substituents NHR and CHOHMe, respectively (only the twist conformation is depicted in Scheme 4). Compounds (13)—(15) display intermediate values (4.4—6.7) for the *trans*-interactions ^3J(2,3), indicating that rapid inversion between opposite conformations occurs. A simple calculation performed by using a value of 12 Hz [29] for a *trans*-pseudodiaxial coupling and a value of 1.5 Hz for a *cis*-pseudodiequatorial coupling between H-2 and H-3 yields the approximate amounts of the individual conformers (see Scheme 4). For compounds (13) and (14) the conformation with a pseudoaxial orientation of the substituents NHR and CHOHMe is more abundant (*ca.* 70%) than that with a pseudoequatorial orientation, while the D-*xylo*-derivative (15) displays approximately equal amounts of conformers with opposite conformations $^3T_4$ (^3E) and $^4T_3$ (E_3).

Discussion of ^{13}C *spectra.* The ^{13}C chemical shifts of all the 3-benzoylamino-2,3,6-trideoxy-L-hexoses are reported in Table 4 together with the approximate percentages of the tautomeric mixtures obtained after *ca.* 1 week. To our knowledge only the spectrum of the methyl glycoside of daunosamine hydrochloride (methyl 3-amino-2,3,6-trideoxy-L-α-*lyxo*-pyranoside hydrochloride) has been reported [31] with the assignment of all the ^{13}C resonances.

TABLE 4

^{13}C Chemical shifts of 3-benzoylamino-2,3,6-trideoxy-L-hexoses [a]

Compd.	C-1	C-2	C-3	C-4	C-5	C-6	% [b]
(17a)	89.8	36.9	48.3	74.2	67.6	18.3	85
(17b)	93.5	38.9	51.5	73.4	72.8	18.3	15
(18a)	90.3	30.3	45.6	68.2	65.4	17.2	52
(18b)	94.2	33.0	49.6	66.9	70.9	17.2	32
(19a)	90.4	28.8	47.7	67.6	62.5	16.5	64
(19b)	91.6	31.8	50.4	66.9	68.6	17.0	36
(20a)	89.9	33.8	46.8	71.3	65.0	17.9	16
(20b)	91.2	*c*	48.4	70.9 [d]	69.6 [d]	18.6	10
(18c)	96.9 [e]	*c*	*c*	86.8 [f]	67.6	19.5	8
(18d)	97.2 [e]	*c*	*c*	85.1 [f]	66.5	19.5	8
(20c)	97.1 [g]	39.0 [h]	49.7	85.7	66.8	18.9 [i]	34
(20d)	96.9 [g]	40.3 [h]	49.7	87.0	67.6	19.1 [i]	40

[a] Chemical shifts in p.p.m. from internal Me_4Si; solvent $(CD_3)_2SO$. [b] Tautomeric mixture after *ca.* 1 week. [c] Peaks not assigned. [d-i] Assignments may be interchanged.

The variations of the chemical shifts of the carbon atoms in the pyranose ring according to the orientation of the hydroxy-groups have been studied extensively by several authors.[32-34] They showed that an axial substituent is associated with larger shielding of the ^{13}C nuclei which are α, β, and γ to the substituent, than is an equatorial one. An average value of 3.5 p.p.m. is representative of most of the shielding changes associated with these configurational inversions. However several deviations were observed. In particular Perlin *et al.*[32] found that in the series of pento- and hexo-pyranoses inversion of configuration at C-4 has little impact on the shielding of C-4 (0.3—1.2 p.p.m.) and C-5 (−1.2—0.8 p.p.m.). On the contrary, in the 3-benzoylamino-2,3,6-trideoxypyranoses the change from equatorial to axial orientation of OH-4, *i.e.* in (20a,b) *vs.* (19a,b) and in (17a,b) *vs.* (18a,b), induces much stronger shielding of C-4 (4—6.4 p.p.m.) and C-5 (*ca.* 2 p.p.m.). In addition the shielding effect on C-2 is also much larger (5—6 p.p.m. against 2—3 p.p.m. for the reported [32] pento- and hexo-pyranoses).

The small quantity of material available for the 3-benzoylamino-2,3,6-trideoxyfuranoses (18c,d) and (20c,d) precluded ^1H selective decoupling experiments for the assignment of the ^{13}C chemical shifts. The attribution of the C-5 signal for the α- and β-anomers was made by using the low-field δ-effect exerted by OH-1 *cis* to C-5. The same effect was found in a series of methyl glycosides,[35] which display a deshielding C-5 by 0—2.3 p.p.m. in the *cis*- as compared with the *trans*-arrangement of the substituents at C-1 and C-4. Furthermore, since (20c) is present in solution in a slightly greater amount than (20d), the differences in signal intensities allow the assignment of all the signals, except those which are too close to each other.

The ^{13}C chemical shifts of the γ- and δ-lactones are reported in Table 5. The chemical shift of the carbonyl carbon C-1 is diagnostic for distinguishing between γ- and δ-lactones; in six-membered rings the C-1 signal is shifted upfield by about 5 p.p.m. with respect to the five-membered ring structures. In the γ-lactone derivatives the *cis*- (as compared with the *trans*-) arrangement of the C-3 and C-4 substituents is associated with larger shielding of C-4 and C-5. These effects were attributed to steric compression [35] caused by the two *cis*-substituents and are diagnostic for the stereochemistry in substituted five-membered rings. In contrast the chemical shifts of C-3 are not simply related to the *cis*- or *trans*-arrangement of C-3 and C-4 substituents, as already observed for substituted cyclopentanols.[35]

TABLE 5

^{13}C Chemical shifts of 3-benzoylamino-2,3,6-trideoxyhexono-δ- and γ-lactones [a]

Compd.	C-1	C-2	C-3	C-4	C-5	C-6
(10)	169.7	35.3	49.4	71.5	76.6	18.0
(11)	171.3	31.8	48.9	67.8	75.4	17.1
(13)	175.7	34.5	48.3	88.4	66.4	19.2
(14)	175.5	35.1	45.6	88.9	66.1	18.4
(15)	175.1	34.4	47.3	84.2	64.3	19.3
(16)	175.0	35.7	48.0	84.6	63.9	19.7

[a] Chemical shifts in p.p.m. from internal Me_4Si, solvent $(CD_3)_2SO$.

Inversion of configuration at C-3 and C-4 for δ-lactones induces variations in the chemical shifts of ring carbons which are sensibly smaller than those observed in the analogous pyranoses. In particular, comparing the L-*arabino*- (10) with the L-*xylo*-δ-lactone (11), C-5 is shielded only by 1.2 p.p.m. as against 4.2 p.p.m. found for β-L-*arabino*- (17b) relative to β-L-*xylo*-pyranose (19b). These reduced steric effects in δ-lactones are indicative of some conformational mobility, which is also indicated by the values of the ^1H coupling constants given above.

EXPERIMENTAL

The ^1H n.m.r. spectra of the hexoses were recorded on Bruker WH-400 and WH-270 spectrometers (concentration *ca.* 10 mg ml^{-1}). All samples were dissolved in $(CD_3)_2SO$ except the L-*ribo*-amino-sugar which was dissolved also in pyridine. The convolution difference method for resolution enhancement of the signals was employed to obtain accurate values of the coupling constants (± 0.2 Hz). The ^1H spectra of γ- and δ-lactones and the ^{13}C spectra of all compounds were measured with a Varian XL-100 spectrometer. The proton spectra were run in $CDCl_3$ for the γ-lactones and in $(CD_3)_2CO$ for the δ-lactones (concentration range 2—5 mg ml^{-1}). The ^{13}C spectra of all compounds were obtained in $(CD_3)_2SO$ (concentration of *ca.* 70 mg ml^{-1}). The assignment of most of the carbon signals was made by ^1H selective heteronuclear decoupling experiments.

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