Synthesis of Diastereomerically Pure 4′-Alkoxy-α-(L)- and -β(D)-nucleosides and their Conformational Analysis by 500 MHz ^{1}H NMR Spectroscopy

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Electrophilic addition reactions of alcohols to 4′,5′-unsaturated nucleosides **1** and **2** under mild, acidic conditions have produced various diastereomerically pure 4′-alkoxy-β(D)- and 4′-alkoxy-α(L)-5′-deoxy-nucleosides **3–11** in good yields. The steric hindrance exerted by the bulk of the alcohol was the principal factor governing the distribution of diastereomers in the reactions of **1**. The distribution was, however, reversed when **2** was used as the substrate. The synthesis of various 4′-alkoxy-4′-hydroxymethyl-β(D)-/α(L)-nucleosides **12–15** has been achieved by the action of *m*-chloroperbenzoic acid and an alcohol on **1** and **2**. This reaction followed a reaction sequence involving the oxidation of the double bond followed by the alcohol-promoted ring-opening of the epoxide ('oxidation–substitution'). This oxidation–substitution reaction did not show the same striking diastereoselectivity owing to the fact that the proportion of the final products was dictated at the first radical-oxidation step, which showed almost equal diastereofaciality. The configuration at C4′ was assigned with the help of 1D differential NOE experiments at 500 MHz at 20°C. Clear NOEs between H3′ and 4′-methyl and between H6 and 4′-methyl were observed for **3b**, **4b**, **6b** and **7b** suggesting a β(D) configuration for the methyl at C-4′. The absence of these NOEs in **3a**, **4a**, **5**, **6a** and **7a** allowed us to assign the C-4′ substituent in the α(L) configuration. Observed 1D differential NOEs between H6 and H5′/5″ and between H3′ and H5′/5″ in **13b**, **14b** and **15b** suggested that the 4′-alkoxy groups are in the α(L) configuration. Absence of these NOEs in compounds **13a**, **14a** and **15a** suggested that the 4′-alkoxy groups are in the β(D) configuration. The 4′-alkoxy substituted ribose rings in compounds **3a**, **4a**, **5**, **6a** are biased to a South-type conformation in the $N \rightleftarrows S$ equilibrium (>ca. 90%) (Φ_m for **3a**, **4a**, **5**, **6a** $\approx 42°$, P_S are around 160–170°), and the 4′-triazolo-substituted compound **7b** also seems to adopt a modified South-type conformation (>ca. 80%) (Φ_m is $<35°$, $P_S \approx 180°$). The pseudorotamer population of the constituent sugar in the $N \rightleftarrows S$ equilibrium in compounds **13a**, **14a** and **15a** is biased to the *S* conformer (ca. 80%) with $\Phi_m \approx 42°$ and P_S of around 160–170°. All 4′-alkoxynucleosides reported herein have been found to have an *anti* conformation across their glycosidic bonds.

Dedicated to Professor Salo Gronowitz on the occasion of his 65th birthday.

The human immunodeficiency virus (HIV) is the causative agent of the acquired immune deficiency syndrome (AIDS).[1–4] Since the discovery of AIDS, 3′-azidothymidine and 2′,3′-dideoxyinosine have been successfully employed as chemotherapeutic agents,[5–9] and many other 2′,3′-dideoxynucleosides and their 3′-substituted derivatives are also presently undergoing clinical trial. The biological activities of 4′-modified nucleosides as potential anti-HIV agents have, however, been little explored because it is chemically difficult to introduce substituents at C-4′.[10–19] The pioneering work by Moffatt *et al.*[11–16] first demonstrated that 4′,5′-unsaturated nucleosides are useful intermediates to access 4′-fluoro- and 4′-methoxy-nucleosides via electrophilic addition reactions with pseudohalides. Although it is well established that enol ethers, in general, are active substrates toward electrophilic addition,[20–23] the difficulty of employing such reactions using 4′,5′-unsaturated nucleosides is due to the fact that they are very sensitive to traces of acid[24–30] which is normally the catalyst in electrophilic addition reactions. We now report that, despite the acid-sensitive nature of 4′,5′-unsaturated nucleosides **1** and **2**, it has been possible to perform electrophilic addition to alcohols under appropriate acidic conditions[31] to give various diastereomeric 4′-alkoxy-4′-methyl-β(D)- and 4′-alkoxy-4′-methyl-α(L)-nucleosides **3–11** in good yields. We also report the synthesis of various 4′-alkoxy-4′-hydroxymethyl-β(D)/α(L) nucleosides **12–15** by the action of *m*-chloroperbenzoic acid and alcohol, through the intermediacy of putative 4′,5′-epoxy nucleosides (Scheme 1). These reactions are based upon the original observation of Sweet and Brown[32] who first noted that

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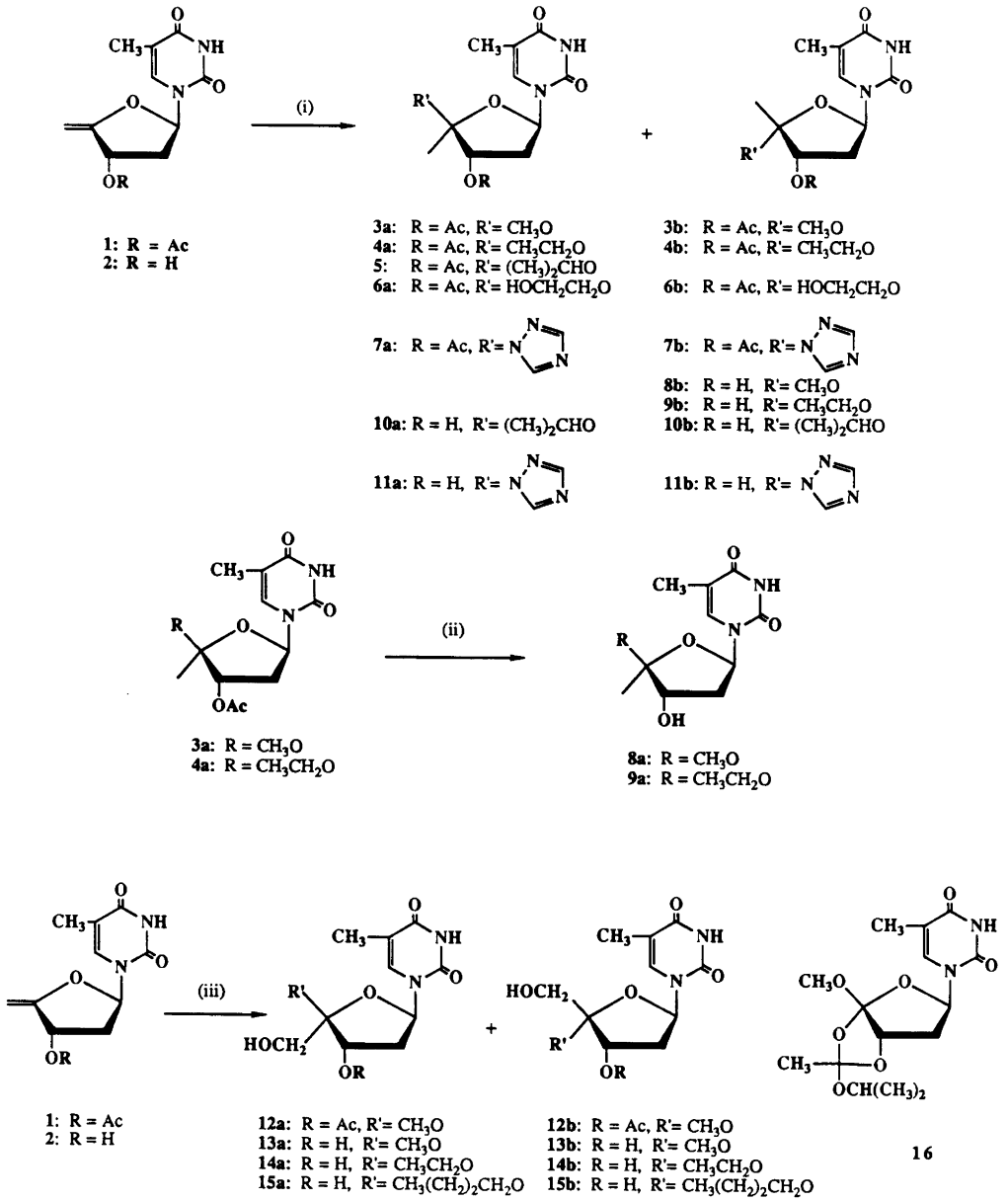
the oxidation of 2,3-dihydrofuran or 2,3-dihydropyran with perbenzoic or *m*-chloroperbenzoic acid in the presence of an alcohol gives *trans*-2-alkoxy-3-hydroxytetrahydrofurans and *trans*-2-alkoxy-3-hydroxytetrahydropyrans in moderate-to-high yields.

Acid-catalysed addition reactions. The starting material, 1-(5′-deoxy-3′-*O*-acetyl-β-*erythro*-pent-4′-enofuranosyl) thymine (**1**), was parepared using a published procedure.[11,33] Alcohols, such as methanol, ethanol, isopropyl alcohol and ethylene glycol have been demonstrated to react with **1**, catalysed by acetic acid or boron trifluoride–diethyl ether, giving diastereomeric mixtures of the corresponding 4′-alkoxy-β(D)-/α(L)-nucleosides in good yields. Reaction of **1** with methanol in the presence of boron trifluoride–diethyl ether gave a diastereomeric mixture of 4′-methoxy-α(L)- (41%) **3a** and 4′-methoxy-β(D)- (27%) **3b** products. Reaction of **1** with ethanol under identical conditions afforded the diastereomeric mixture of 4′-ethoxy-α(L)- **4a** (75%) and 4′-ethoxy-β(D)- **4b** (8%) nucleosides. Reaction of **1** with isopropyl alcohol gave, however, only 4′-isopropoxy-α(L)-nucleoside **5** (85%) in a diastereospecific manner. The addition of ethylene glycol to **1** gave a diastereomeric mixture consisting of **6a** (43%) and **6b** (5%). These results suggested that the distributions of the α(L) versus β(D) products in the addition reactions with **1** were controlled both by the steric bulk of the alkyl moiety (R′) in the alcohol (R′-OH) and the equilibrium population of 'open' cation (**A**) versus acyloxonium ion (**B**) (Fig. 1) as reactive



Scheme 1. (i) AcOH or BF_3–Et_2O–alcohol and benzene; (ii) 80% AcOH; (iii) *m*-chloroperbenzoic acid and alcohol–CH_2Cl_2.

intermediates. In general, the 'open' cation (**A**), which is stabilized by the participation of the lone-pair of endocyclic O-4,[12] is likely to be attacked both from the α- or β-face by alcohol complexed by boron trifluoride ($R'OBF_3^-$). The diastereoselective β-attack on the 'open' cation (**A**) may also take place with the bulky alcohol owing to the steric hindrance of 3′-acetoxy group. The acyloxonium ion (**B**),[12] on the other hand, should only promote the diastereospecific β-attack. Larger R′ in R′-OH, as in isopropyl alcohol, gives the α(L)-nucleoside as the sole reaction product owing to the attack at the β-face of the acyloxonium ion (**B**) and this β-attack is also clearly facilitated even on the 'open' cation (**A**) owing to the steric hindrance from the 3′-acetoxy group at the α-face. Note that the ratio of α(L) versus β(D) products was found to be around 3:2 in the reaction with methanol, while it turned out to be 10:1 in the reaction with the bulky ethanol or ethylene glycol. In fact, the isolation of the 3′,4′-β(D)-isopropoxyethylidene derivative **16**[12] (*vide infra*) constitutes direct evidence of the formation of the acyloxonium ion (**B**).

In order to explore the steric and electronic effects exerted by the 3′-*O*-acetyl group in **1** on the electrophilic addition reactions, comparable Lewis-acid catalysed reactions on **2** were subsequently performed. In this set of reactions, *the distribution of diastereomers was reversed.* When methanol or ethanol was reacted with **2** in the presence of a catalytic amount of Lewis acid, it was found that only 4′-methoxy-β(D)- **8b** (68%) or 4′-ethoxy-β(D)- (73%) nucleoside was produced in a *diastereospecific manner*. The reaction of isopropyl alcohol with **2** however, gave both **10a** {[α(L)], 17%} and **10b** {[β(D)], 29%}.

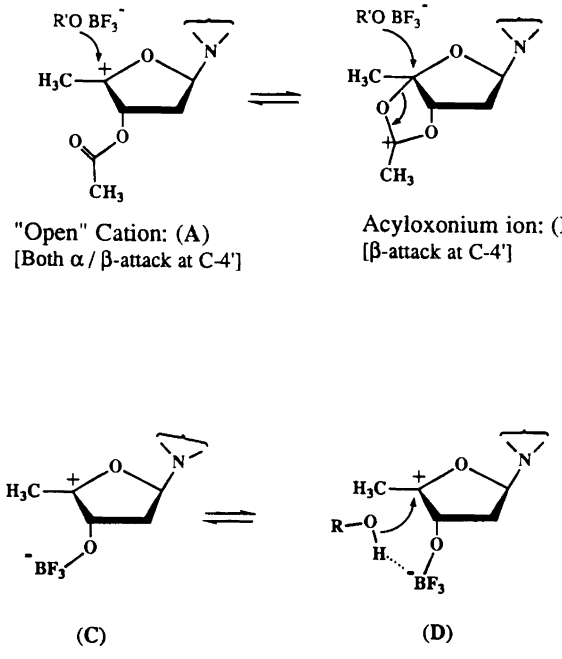


Fig. 1.

It is probable that the 3′-hydroxy group in **2** complexes with boron trifluoride–diethyl ether to give the intermediate (**C**) (Fig. 1) which electrostatically attracts the hydroxy group of smaller R–OH (as in methanol or ethanol) preferentially [shown in intermediate (**D**) in Fig. 1)] and orchestrates an α-attack at C-4′ to give the diastereospecific β(D) product. Larger R–OH (as in isopropyl alcohol) may be less easily attracted by the [BF_3–O(3′)-]-complex in intermediate (**D**), and thus would give more β-face attack than methanol or ethanol.

Reactions of 1,2,4-triazole with both **1** and **2** have been also performed. Under identical reaction conditions in acetonitrile, **1** gave α(L)- **7a** and β(D)- **7b** in ~32% and ~23% yields, respectively, while the reaction of **2** gave predominantly **11b** {[β(D)], 45%} along with a minor amount of **11a** {[α(L)], 7%}. The reaction of 1,2,4-triazole with **2** seems to follow the same course as the reactions of the alcohols with **2**. Similar reaction of **1** or **2** with imidazole or tetrazole was unsuccessful.

Boron trifluoride–diethyl ether catalysed electrophilic addition was found to be faster than with any protic acid. For example, use of a catalytic amount of acetic acid required a few days of boiling at reflux to drive the reaction to completion. Identical reactions with boron trifluoride–diethyl ether were, however, complete within only 2 h at room temperature. Both reaction conditions gave stereochemically identical products but BF_3–Et_2O-promoted reactions gave products with improved yields.

Oxidation–substitution reactions. The treatment of **1** with *m*-chloroperbenzoic acid in the presence of different alcohols at room temperature gave a complex diastereomeric mixture of 4′-alkoxy-4′-hydroxymethyl-α(L)-/β(D)-nucleosides along with by-products arising from to the neighbouring-group participation from the 3′-*O*-acetyl group. Reaction of **1** with isopropyl alcohol under identical conditions gave only the 3′,4′-β(D)-isopropoxyethylidene derivative **16**.[12] Clearly, **16** was formed owing to the participation of the neighbouring 3′-*O*-acetyl group through the participation of acyloxonium ion (**B**).[12] To overcome this problem, all oxidation–substitution reactions with different alcohols in the presence of *m*-chloroperbenzoic acid were performed on **2** to give both α(L)- [**13a** (35%), **14a** (33%), **15a** (22%)] and β(D)-diastereomers [**13b** (28%), **14b** (29%), **15b** (21%)]. These oxidation–substitution reactions did not show the striking diastereoselectivity found in the electrophilic addition reactions (*vide supra*). This is most probably due to the fact that the epoxidation of 4′,5′-double bond in **1** first gave almost an equal amount of diastereomeric α(L)- and β(D)-epoxides which, in the second step, were opened up by the action of the alcohol to give α(L)- (**13a–15a**) and β(D)-nucleosides (**13b–15b**). We have noted, however, that this oxidation–substitution reaction competes with the *m*-chloroperbenzoic acid promoted electrophilic addition of alcohols; *m*-chloroperbenzoic acid was therefore added last in the reaction in order to avoid the formation of by-product.

Table 1. Chemical shifts (δ) at different temperatures of compounds **3a–7b**[a] in $CDCl_3$ at 500 MHz (internal reference set at 2.00 ppm for CH_3CN).

	3a		**3b**		**4a**		**4b**		**5a**		**6a**		**6b**		**7a**		**7b**	
	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K
H1′	6.64	6.63	6.18	6.19	6.64	6.61	6.17	6.11	6.56	6.53	6.61	6.61	6.24	6.23	6.33	6.40	6.68	6.67
H2′	2.43	2.47	2.36	2.38	2.46	2.48	2.30	2.26	2.38	2.44	2.48	2.53	2.36	2.41	2.73	2.79	3.03	3.00
H2″	2.35	2.39	2.53	2.56	2.36	2.39	2.43	2.38	2.30	2.38	2.32	2.38	2.51	2.57	2.79	2.80	2.44	2.50
H3′	5.19	5.25	5.07	5.11	5.21	5.26	5.05	5.07	5.14	5.23	5.25	5.32	5.03	5.14	5.72	5.74	5.69	5.86
5′-Me	1.38	1.43	1.54	1.57	1.40	1.45	1.58	1.55	1.41	1.50	1.40	1.47	1.53	1.61	1.80	1.85	1.89	1.92
H6	7.27	7.31	7.01	7.03	7.34	7.40	7.00	6.96	7.63	7.67	7.46	7.51	6.98	7.03	7.08	7.09	7.44	7.26
5-Me	1.92	1.96	1.95	1.97	1.93	1.96	1.97	1.94	1.89	1.96	1.90	1.96	1.92	1.97	1.92	1.97	1.82	1.86
Ac	2.12	2.14	2.14	2.15	2.13	2.14	2.11	2.02	2.09	2.13	2.12	2.15	2.12	2.14	2.06	2.11	2.18	2.20
(a)	3.31	3.36	3.36	3.38	3.60	3.65	3.67	3.68	4.02	4.13	3.66	3.72	3.61	3.69	7.98	8.00	8.05	8.07
(b)					1.23	1.26	1.25	1.24	1.14	1.24	3.80	3.83	3.75	3.79	8.20	8.22	8.34	8.37

[a] For **3a** and **3b** (a) is MeO, for **4a** and **4b** (a) is CH_3CH_2O– and (b) is CH_3CH_2O–, for **5a** (a) is $(CH_3)_2CHO$– and (b) is $(CH_3)_2CHO$– for **6a** and **6b** (a) is $HOCH_2CH_2O$– and (b) is $HOCH_2CH_2O$–, for **7a** and **7b** (a) and (b) are H1 and H3 of the triazole ring.

Assignment of configuration of C4′ center in 4′-modified nucleosides and their conformational studies

(*i*) *Assignment of C-4′ configuration in 5′-deoxy derivatives* **3–7**. The configuration at C-4′ was assigned with the help of 1D differential NOE experiments at 500 MHz at 20°C. Clear NOEs between H3′ and 4′-methyl and between H6 and 4′-methyl were observed for **3b** (2.2%), **4b** (1.2%), **6b** (1.6%) and **7b** (0.3%). These NOEs were absent in **3a**, **4a**, **5**, **6a** and **7a**. These NOEs led us to assign the 4′-methyl to an 'up' [4′-β(D)] configuration in compounds **3b**, **4b**, **6b** and **7b** and to a 'down' [4′-α(L)] configuration in **3a**, **4a**, **6a**, **5** and **7a**. Roberts *et al.*[34] have shown that the chemical shift of a carbon atom in ^{13}C NMR spectroscopy depends on the steric crowding. Subsequently, Moffatt *et al.*[12] have used the comparison of the chemical shift of the 5′-carbon to assign the configuration at C4′ by ^{13}C NMR spectroscopy. In our ^{13}C NMR studies, we have also observed that the 4′-CH_3 in 4′-α(L)-diastereomers are more upfield than in the corresponding 4′-β(D)-diastereomers which also independently corraborate our above NOE data on **3b–7b** {[^{13}C NMR: δ[4′-Me:α(L)/β(D)]: 15.7/18.9, 16.5/19.5, 17.4/–, 16.7/20.1, 20.2/20.6, 15.3/18.1, 16.2/19.3, 17.4/20.2 and 20.8/23.3 in **3**, **4**, **5**, **6**, **7**, **8**, **9**, **10** and **11** respectively}. This comparison of relative shielding/deshielding effects work effectively when the C-4′ substituent is an alkoxy group and 4′-CH_3.

(*ii*) *Configuration of C-4′ in 5′-hydroxymethyl derivatives* **13b**, **14b** *and* **15b**. 1D differential NOEs were observed between H6 and H5′/5″ in **13b**, **14b** and **15b** (3% in **13b**, 2.9% in **14b** and 1.2% for H5′ and 1.5% for H5″ in **15b**) and between H3′ and H5′/5″ (3.4% in **13b**, 6.1% in **14b** and 3.2% in **15b**), suggesting that the 4′-alkoxy groups in these compounds are in a 'down' [4′-α(L)] configuration. None of these NOEs were observed in compounds **13a**, **14a** and **15a** which suggests that the 4′-alkoxy groups are in an 'up' [4′-β(D)] configuration.

(*iii*) *Conformation of the pentofuranose ring in* **3a–7b** *and* **13a–15b**. The conformation of a pentofuranose ring can be described using the pseudorotational concept.[35] The geometry of the ring is described using two parameters: the phase angle of pseudorotation (*P*), and the puckering amplitude (Φ). The ring is known to exist in an equilibrium of two rapidly interconverting conformers which are denoted north (C2′-*exo*, C3′-*endo*) (*N*) and south (C2′-*endo*, C3′-*exo*) (*S*). The chemical shifts and coupling constants of all compounds at two different temperatures [293 K and 333 K for **13a–15b** (Tables 3 and 4) and 273 K and 313 K for **3a–7b** (Tables 1 and 2)] were

Table 2. $^3J_{HH}$ coupling constants (Hz) for compounds **3a–7b**[a] in $CDCl_3$ at different temperatures measured at 500 MHz.

	3a		**3b**		**4a**		**4b**		**5a**		**6a**		**6b**		**7a**		**7b**	
	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K	273 K	313 K
$J_{1'/2'}$	8.3	8.1	3.7	3.7	8.3	8.3	3.7	3.9	8.6	8.3	9.0	8.8	3.7	3.9	12.5	12.5	9.7	9.2
$J_{1'/2''}$	6.7	6.7	8.3	8.1	6.7	6.5	8.1	8.1	6.7	6.5	6.2	6.3	8.3	7.9			5.8	5.8
$J_{2'/2''}$	14.6	14.6	12.7	12.7	14.6	14.3	12.7	12.7	14.3	14.3	14.3	14.3	13.4	13.6			14.1	14.5
$J_{2'/3'}$	4.9	5.1	9.0	9.0	4.9	4.9	8.6	8.6	4.9	4.9	5.1	5.1	8.8	8.6	15.7	15.5	5.8	5.8
$J_{2''/3'}$	0	0.7	9.0	9.0	0	0	8.6	8.1	0	0	0	0	8.8	8.6			0	0

[a] Note that for compound **7a**, Σ 1′ and Σ 3′ are given owing to the overlap of H2′ and H2″.

Table 3. Chemical shift (δ) of compounds **13a–15b**[a] in D_2O at different temperatures measured at 500 MHz (internal reference set at 2.00 ppm for CH_3CN).

	13a		**13b**		**14a**		**14b**		**15a**		**15b**	
δ	293 K	333 K	293 K	333 K	293 K	333 K	293 K	333 K	293 K	333 K	293 K	333 K
H-1′	6.57	6.49	6.20	6.18	6.53	6.47	6.21	6.17	6.50	6.44	6.17	6.15
H-2′	2.56	2.52	2.40	2.40	2.59	2.55	2.40	2.38	2.59	2.55	2.40	2.38
H-2″	2.33	2.33	2.40	2.40	2.32	2.33	2.44	2.42	2.32	2.33	2.45	2.42
H-3′	4.34	4.34	4.58	4.56	4.34	4.35	4.57	4.54	4.35	4.36	4.57	4.53
H-5′	3.84	3.84	3.77	3.76	3.84	3.84	3.78	3.78	3.84	3.84	3.80	3.77
H-5″	3.74	3.75	3.70	3.72	3.75	3.76	3.70	3.71	3.73	3.77	3.70	3.71
H-6	7.45	7.42	7.46	7.43	7.47	7.45	7.49	7.45	7.49	7.46	7.50	7.45
5-CH_3	1.86	1.85	1.81	1.82	1.87	1.86	1.82	1.82	1.86	1.85	1.82	1.81
(a)	3.28	3.27	3.33	3.34	3.61	3.62	3.61	3.62	3.54	3.54	3.65	3.65
					3.53	3.53			3.43	3.44	3.53	3.55
(b)					1.18	1.16	1.15	1.14	1.57	1.54	1.51	1.51
									1.48	1.46		
(c)									1.28	1.27	1.32	1.31
(d)									0.83	0.82	0.85	0.84

[a] Note that for **13a** and **13b** (a) is MeO, for **14a** and **14b** (a) is CH_3CH_2O– and (b) is CH_3CH_2O–, for **15a** and **15b** (a) is $CH_3CH_2CH_2CH_2O$– and (b) is $CH_3CH_2CH_2CH_2CH_2O$–, (c) is $CH_3CH_2CH_2CH_2O$– and (d) is $CH_3CH_2CH_2CH_2O$–.

measured and were used to determine the constituent sugar conformation.

For the use of $^3J_{HH}$ couplings for the conformational analysis of 4′-substituted nucleosides, we were faced with two basic problems: (i) owing to the absence of H-4′, the important $J_{3',4'}$ coupling constant could not be used in the pseudorotational calculations of the sugar ring, (ii) the resonances of the H2′ and H2″ overlap in compounds **7a**, **13b**, **14b** and **15b** which means that only the sums of the couplings to H1′ ($\sum 1' = \sum J_{1',2'+1',2''}$)[36] and H3′ ($\sum 3' = \sum J_{2',3'+3',4'}$)[36] are available for conformational analysis. To circumvent these problems, we additionally used 1D NOE-difference experiments to determine the sugar conformation [$N \rightleftarrows S$ equilibrium] and glycosyl torsion [*syn* ⇄ *anti* equilibrium].

Conformation of the 5′-deoxy derivatives. Since H2′ and H2″ resonances were almost superimposed in these compounds, individual $^3J_{HH}$ cannot be used for pseudorotational calculations; the % population of the south conformer (%*S*)[36] (Table 5) was therefore estimated using eqn. (1).

$$\%S = \left[\left(\sum 1' - 9.8\right)/5.9\right] 100 \qquad (1)$$

A $\sum 1'$ value of 13–16 Hz has been found to indicate a predominance of the *S*-type conformer,[36] while a $\sum 1'$ value of 8–11.5 Hz suggest a predominance of the *N*-type conformer[36] in the $N \rightleftarrows S$ equilibrium. In compounds **3a**, **4a**, **5**, **6a** and **7b**, a $\sum 1'$ value of ca. 15 Hz therefore means that they are in an *S*-type conformation. The $\sum 1'$ value of ca. 11 Hz for **3b**, **4b**, **6b** and **7a** suggest an *N*-type conformation. A graphical method was subsequently used to translate our experimental coupling constants into a rough structural model of the different furan rings. In Fig. 2(a), are shown the calculated dependence of $J_{1'2'}$ and $J_{2'3'}$ on the phase angle of pseudorotation (*P*) at different fixed values of puckering amplitude ($\Phi_m = 39°$, 42°, 45°). The calculations are based on (i) the empirically generalized Karplus equation as developed by Altona *et al.*[37] which relates vicinal proton–proton *J*-coupling constants to proton–proton torsion angles, and (ii) the relations ϕ[H1′–C1′–C2′–H2′] = 121.4° + 1.03v_1 and ϕ[H2′–C2′–C3′–H3′] = 2.4° + 1.06v_2.[38] Closed curves are obtained as *P* varies from 0° (north region) to 180° (south region) to 360° (north region). The experimental data points which are NMR time-averaged *J*-coupling constants ($J_{1'2'}$ are from 7.5–9.5 Hz, and $J_{1'2'}$ are from 4.8–5.8 Hz) in each participating conformer in **3a**, **4a**, **5**,

Table 4. $^3J_{HH}$ coupling constants (Hz) of compounds **13a–15b**[a] in D_2O at different temperatures measured at 500 MHz.

	13a		**13b**		**14a**		**14b**		**15a**		**15b**	
	293 K	333 K	293 K	333 K	293 K	333 K	293 K	333 K	293 K	333 K	293 K	333 K
$J_{1'/2'}$	8.1	8.1	11.4	11.8	8.5	7.9	11.1	12.3	8.0	7.7	10.6	11.4
$J_{1'/2''}$	6.9	6.5			6.9	6.8			6.9	6.8		
$J_{2'/2''}$	14.3	14.6			14.7	14.5			14.8	14.6		
$J_{2'/3'}$	4.9	5.4	17.6	17.0	4.9	5.4	17.8	16.6	4.9	5.4	17.2	17.6
$J_{2''/3'}$	0	0			0	0			0	1.4		
$J_{5'/5''}$	12.5	12.5	12.5	12.4	12.6	12.5	12.6	13.1	12.5	12.5	12.3	12.3

[a] Note that for compounds **13b**, **14b** and **15b** $\sum 1'$ and $\sum 3'$ are given owing to the overlap of H2′ and H2″.

Table 5. Estimations of percentage of south (%*S*) conformer of compounds **3a–7b** and **13a–15b** from calculation of $\sum 1'$.[a,36]

Compound	$\sum 1'^{a}$/Hz	$\%S^{b}$	Compound	$\sum 1'^{a}$/Hz	$\%S^{b}$
3a	15.5	97	**13a**	15	88
3b	11.9	36	**13b**	11.4	27
4a	14.8	85	**14a**	15.4	95
4b	12	37	**14b**	11.1	22
5a	14.8	85	**15a**	14.9	86
6a	15.1	90	**15b**	10.6	14
6b	12	37			
7a	12.5	46			
7b	15	88			

[a] $\sum 1' = J_{1'2'} + J_{1'2''}$. [b] $\%S = [(\sum 1' - 9.8)/5.9]100$ (see Ref. 36).

6a are very close to the south region. This shows that the 4′-alkoxy-substituted ribose rings in compounds **3a**, **4a**, **5**, **6a** are biased towards a south-type conformation in the $N \rightleftarrows S$ equilibrium (>ca. 90%), and the 4′-triazolo-substituted compound **7b** also seems to adopt a modified south-type conformation (>ca. 80%). Clearly, the position of the experimental data points in Fig. 2(a) is determined by the *J*-values in each of the participating conformers in the $N \rightleftarrows S$ conformational equilibrium and their mole fractions at a particular temperature. In the case of a two-state equilibrium, this means that the experimental data points at 293 K are found on the line (conode) that connects the *P*-values for the two participating conformers. It is of interest to note that the experimental data points for **3a**, **4a**, **5**, **6a** are offset from any conode that can be drawn between the points on the curve for $\Phi_m = 39°$ or 42° which suggests that Φ_m for **3a**, **4a**, **5**, **6a** should be in the range 39°–42° while Φ_m for **7b** is expected to be less than 36°. It can be seen from this line of reasoning that the experimental data points for compounds **3a**, **4a**, **5** and **6a** in Fig. 2(a) clearly suggest that they have south-type sugars and their phase angles (P_S) should be around 160–170° while P_S for **7b** should be around 180°.

For compounds **3b**, **4b**, **6b** and **7a** we made similar calculations using $\sum 1'$ and $\sum 3'$ for the reasons stated above [Fig. 2(b)]. An assessment of experimental data show that our coupling constants lie well outside the normal $N \rightleftarrows S$ equilibrium. It is possible that the furan rings in compounds **3b**, **4b**, **6b** and **7a** adopt a modified north-type conformation. Here it can be seen that the 4′-triazolo-substituted compound **7a** have a more 'normal' north-type conformation. A similar conclusion was arrived at upon assessing the 1D differential NOE experiments. A stronger NOE between H6 and H2′ than between H6 and H3′ suggest a south-type conformation for compounds **3a**, **4a**, **5**, **6a** and **7b**. Similarly, a stronger NOE between H6 and H3′ than between H6 and H2′ suggests a north-type conformation for compounds **3b**, **4b** and **6b**. It was not, however, possible to compare the relative NOE strength in compound **7a** since it had a *syn* conformation around the glycosidic bond (*vide infra*).

Conformation of the 5′-hydroxy derivatives. $\sum 1'$ for compounds **13a**, **14a** and **15a** are ca. 15 Hz indicating that

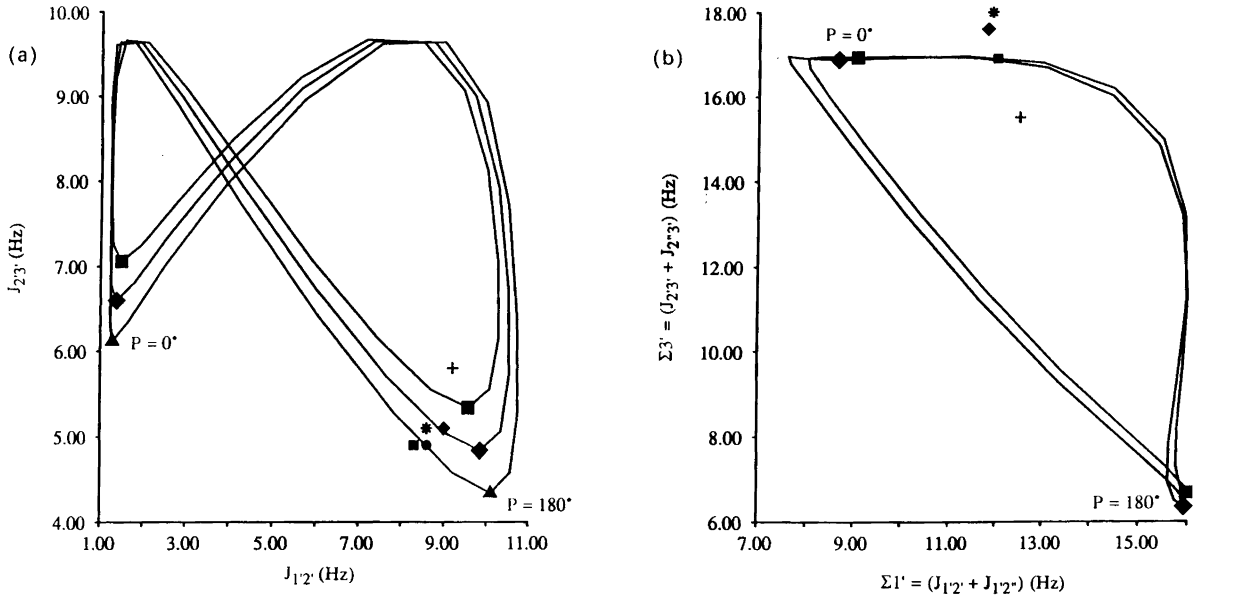


Fig. 2. (a) $J_{1'2'}$ versus $J_{2'3'}$ at different Φ_m values: 36° (■), 39° (◆), 42° (▲). Data points for compounds **3a** (*), **4a** (■), **5** (◆), **6a** (●) and **7b** (+) were obtained from the experimental couplings measured at 500 MHz in $CDCl_3$ at 293 K (Table 2). From the plot it can be seen that compounds **4a** and **6a** have a Φ_m of approximately 42°, the Φ_m of **3a** and **5** is approximately 39° and that of **7b** less than 36°. (b) $\sum 1'$ versus $\sum 3'$ at different Φ_m values: 36° (■), 39° (◆). Data points for compounds **3b** (*), **4b** (■), **6b** (◆) and **7a** (+) were obtained from the experimental couplings measured at 500 MHz in D_2O at 293 K (Table 2). The plot shows that all compounds have a Φ_m of less than 36°.

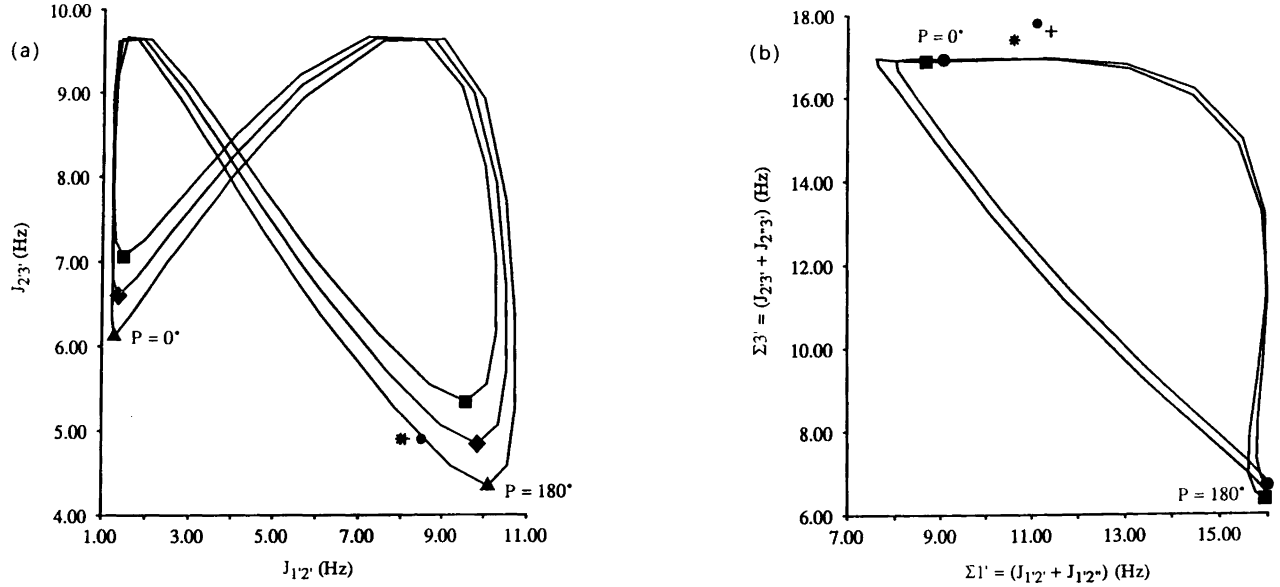


Fig. 3. (a) $J_{1'2'}$ versus $J_{2'3'}$ at different Φ_m values: 36° (■), 39° (◆), 42° (▲). Data points for compounds **13a** (+), **14a** (●) and **15a** (*) were obtained through the experimental couplings measured at 500 MHz in $CDCl_3$ at 293 K (Table 3). It can be seen from the plot that all compounds have a Φ_m of approximately 42°. (b) $\sum 1'$ versus $\sum 3'$ at different Φ_m values: 36° (●), 39° (■). Data points for compounds **13b** (+), **14b** (●) and **15b** (*) were obtained from the experimental couplings measured at 500 MHz in D_2O at 293 K (Table 3). The plot shows that all compounds have a Φ_m of less than 36°.

they have a south-type conformation. $\sum 1'$ for **13b**, **14b** and **15b** are smaller (ca. 11 Hz) indicating a north-type of conformation. We have also used the graphical method for these compounds. The experimental coupling constants observed for compounds **13a**, **14a** and **15a** suggest the predominance of the *S* conformer (ca. 80%) in the $N \rightleftarrows S$ equilibrium [Fig. 3(a)]. Again the puckering amplitude seems to be around 42° with P_S in the range 160–170°. From a perusal of the experimental data for compounds **13b**, **14b** and **15b** in a plot of *J* versus *P*, the same behaviour as for compounds **3b**, **4b**, **6b** and **7a** is observed, i.e., the coupling constants lie outside the normal $N \rightleftarrows S$ equilibrium [Fig. 3(b)]. It is again likely that the furan rings in compounds **13b**, **14b** and **15b** adopt a modified north-type conformation. The conformation of the furan rings was also substantiated by the 1D differential NOE experiments. For compounds **13b**, **14b** and **15b**, the NOE between H6 and H3′ was stronger than that between H6 and H2′ indicating a north-type conformation. In compounds **13a**, **14a** and **15a**, we have, however, observed a stronger NOE between H6 and H3′ than between H6 and H2′ suggesting a south-type conformation. It should be noted that this conformation of the furan ring always forces the 4′-alkoxy substituent into a more axial-type orientation; the 4′-triazolo group, however, seems to prefer a more equatorial-type orientation.

(iv) Conformation around the glycosidic bond. The conformation around the glycosidic bond has been determined for all compounds using 1D differential NOE experiments. If the NOE between H6 and H2′ (for south-type sugars) or H3′ (for north-type sugars) is stronger than that between H6 and H1′ we assigned an *anti* conformation rather than a *syn* conformation.[39] All compounds except **7a** were found to be in an *anti* conformation. In compound **7a** we observed a strong NOE between H6 and H1′ (8.8%) and weak NOEs between H6 and H2′ and H6 and H3′ (both ca. 0.8%) leading us to assign a *syn* conformation. The *syn* conformation is probably due to steric crowding because of the orientation of triazolo-group on the β-face of the sugar.

Experimental

^1H NMR spectra were recorded (on the δ scale) with a Jeol 90Q spectrometer at 90 MHz or at 500 MHz with a Bruker 500 AMX NMR spectrometer using Me_4Si (0.0 ppm) as the internal standard. ^{13}C NMR spectra were recorded at 22.5 MHz using ^1H-coupled and ^1H-decoupled or INEPT modes. A Jeol DX 303 instrument was used for recording the high resolution mass spectra. TLC was carried out using Merck precoated silica gel F_{254} plates. The column chromatographic separations were carried out using Merck G60 silica gel.

1-(-O-Acetyl-2,5-dideoxy-4-methoxy-α-L-lyxofuranosyl) thymine (**3a**) *and 1-(3-O-acetyl-2,5-dideoxy-4-methoxy-β-D-ribofuranosyl)thymine* (**3b**). To a solution of **1** (133 mg, 0.5 mmol) in a mixture of methanol (5 ml) and benzene (15 ml) was added one drop of boron trifluoride–diethyl ether and the reaction was stirred at room temperature for 2 h. Then the reaction mixture was

concentrated to 5 ml. Toluene (2 × 10 ml) was added and concentrated to 5 ml. The residue was separated on a silica gel column to give **3a** (72 mg, 41%) and **3b** (41 mg, 27%).

Compound **3a**: ^{1}H NMR ($CDCl_3$): 9.53 (br, 1 H, NH), 7.32 (d, 1 H, H-6), 6.66 (dd, $J_{1',2'} = 7.1$ Hz, $J_{1',2''} = 8.1$ Hz, H-1'), 5.24 (dd, $J_{2',3'} = 2.1$ Hz, $J_{2'',3'} = 4.1$ Hz, 1 H, H-3'), 3.35 (s, 3 H, OCH_3), 2.42 (m, 2 H, H-2', H-2''), 2.14 (s, 3 H, Ac), 1.96 (d, 3 H, 5-CH_3), 1.41 (s, 3 H, H-5'). ^{13}C NMR ($CDCl_3$): 135.4 (d, $J_{CH} = 177.5$ Hz, C-6), 84.3 (d, $J_{CH} = 175.2$ Hz, C-1'), 77.5 (d, $J_{CH} = 162.9$ Hz, C-3'), 49.2 (q, $J_{CH} = 142.8$ Hz, OCH_3), 36.1 (t, $J_{CH} = 135.4$ Hz, C-2'), 20.8 (q, $J_{CH} = 129.8$, Ac), 15.7 (q, $J_{CH} = 128.1$ Hz, C-5'), 12.6 (q, $J_{CH} = 129.2$ Hz, 5-CH_3. MS (FAB$^-$): Calc. for ($M - H^-$) 297.1087. Found 297.1090.

Compound **3b**: ^{1}H NMR ($CDCl_3$): 9.31 (br, 1 H, NH), 7.04 (s, 1 H, H-6), 6.21 (dd, $J_{1',2'} = 4.1$ Hz, $J_{1',2''} = 7.4$ Hz, 1 H, H-1'), 5.11 (t, $J_{2',3'} = 8.9$ Hz, 1 H, H-3'), 3.37 (s, 3 H, OCH_3), 2.44 (m, 2 H, H-2', H-2''), 2.15 (s, 3 H, Ac), 1.97 (s, 3 H, 5-CH_3), 1.55 (s, 3 H, H-5'). ^{13}C NMR ($CDCl_3$): 134.9 (d, $J_{CH} = 180.8$ Hz, C-6), 82.2 (d, $J_{CH} = 171.8$ Hz, C-1'), 75.5 (d, $J_{CH} = 161.7$ Hz, C-3'), 48.9 (q, $J_{CH} = 143.4$ Hz, OCH_3), 34.9 (t, $J_{CH} = 136.0$ Hz, C-2'), 20.8 (q, $J_{CH} = 130.8$ Hz, Ac), 18.9 (q, $J_{CH} = 128.0$ Hz, C-5'), 12.5 (q, $J_{CH} = 132.5$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 297.1087. Found 297.1077.

1-(3-O-Acetyl-2,5-dideoxy-4-ethoxy-α-L-lyxofuranosyl)-thymine (**4a**) *and 1-(3-O-acetyl-2,5-dideoxy-4-ethoxy-β-D-ribofuranosyl)thymine* (**4b**). To a solution of **1** (133 mg, 0.5 mmol) in a mixture of absolute ethanol (5 ml) and benzene (20 ml) was added one drop of boron trifluoride–diethyl ether and the reaction was stirred at room temperature for 2 h. Then the reaction mixture was worked up and purified following a procedure described for **3a** and **3b** to give **4a** (117 mg, 75%) and **4b** (12 mg, 8%).

Compound **4a**: ^{1}H NMR ($CDCl_3$): 9.61 (br, 1 H, NH), 7.39 (d, 1 H, H-6), 6.64 (t, $J_{1',2'} = 7.4$ Hz, 1 H, H-1'), 5.27 (d, $J_{2',3'} = 4.9$ Hz, 1 H, H-3'), 3.64 (q, $J = 7.1$ Hz, 2 H, OCH_2CH_3), 2.44 (m, 2 H, H-2', H-2''), 2.15 (s, 3 H, Ac), 1.96 (d, 3 H, 5-CH_3), 1.44 (s, 3 H, H-5'), 1.26 (t, 3 H, OCH_2CH_3). ^{13}C NMR ($CDCl_3$): 135.4 (d, $J_{CH} = 183.1$ Hz, C-6), 84.3 (d, $J_{CH} = 174.1$ Hz, C-1'), 77.5 (d, $J_{CH} = 161.8$ Hz, C-3'), 57.5 (t, $J_{CH} = 144.4$ Hz, OCH_2CH_3), 36.2 (t, $J_{CH} = 134.8$ Hz, C-2'), 20.8 (q, $J_{CH} = 129.2$ Hz, Ac), 16.5 (q, $J_{CH} = 128.1$ Hz, C-5'), 15.1 (q, $J_{CH} = 129.6$ Hz, OCH_2CH_3), 12.4 (q, $J_{CH} = 128.2$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 311.1243. Found 311.1270.

Compound **4b**: ^{1}H NMR ($CDCl_3$): 8.64 (br, 1 H, NH), 6.97 (d, 1 H, H-6), 6.14 (dd, $J_{1',2'} = 4.2$ Hz, $J_{1',2''} = 7.6$ Hz, 1 H, H-1'), 4.98 (t, $J_{2',3'} = 8.8$ Hz, 1 H, H-3'), 3.57 (m, 2 H, OCH_2CH_3), 2.42 (m, 2 H, H-2', H-2''), 2.07 (s, 3 H, Ac), 1.96 (d, 3 H, 5-CH_3), 1.49 (s, 3 H, H-5'), 1.16 (t, $J = 7.1$ Hz, 3 H, OCH_2CH_3). ^{13}C NMR ($CDCl_3$): 134.4 (d, $J_{CH} = 179.7$ Hz, C-6), 81.8 (d, $J_{CH} = 171.5$ Hz, C-1'), 75.3 (d, $J_{CH} = 150.5$ Hz, C-3'), 56.7 (t, $J_{CH} = 141.7$ Hz, OCH_2CH_3), 34.7 (t, $J_{CH} = 135.9$ Hz, C-2'), 20.4 (q, $J_{CH} = 129.7$ Hz, Ac), 19.6 (q, $J_{CH} = 126.9$ Hz, C-5'), 15.1 (q, $J_{CH} = 129.2$ Hz, OCH_2CH_3), 12.1 (q, $J_{CH} = 128.2$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 311.1243. Found 311.1259.

1-(3-O-Acetyl-2,5-dideoxy-4-isopropoxy-α-L-lyxofuranosyl)thymine (**5**). To a solution of **1** (133 mg, 0.5 mmol) in a mixture of isopropyl alcohol (2 ml) and benzene (15 ml) was added one drop of boron trifluoride–diethyl ether and the reaction was stirred at room temperature for 1 h. The reaction mixture was then worked up and purified following a procedure described for **3a** and **3b** to give **5** (138 mg, 85%). ^{1}H NMR ($CDCl_3$): 9.17 (br, 1 H, NH), 7.68 (d, 1 H, H-6), 6.56 (dd, $J_{1',2'} = 7.1$ Hz, $J_{1',2''} = 7.5$ Hz, 1 H, H-1'), 5.23 (dd, $J_{2',3'} = 2.3$ Hz, $J_{2'',3'} = 3.6$ Hz, 1 H, H-3'), 4.11 [qq, $J = 6.1$ Hz, 1 H, $OCH(CH_3)_2$], 2.41 (m, 2 H, H-2', H-2''), 2.14 (s, 3 H, Ac), 1.96 (d, 3 H, 5-CH_3), 1.48 (s, 3 H, H-5'), 1.23 [d, 6 H, $OCH(CH_3)_2$]. ^{13}C NMR ($CDCl_3$): 136.2 (d, $J_{CH} = 185.4$ Hz, C-6), 84.4 (d, $J_{CH} = 171.9$ Hz, C-1'), 77.7 (d, $J_{CH} = 164.0$ Hz, C-3'), 66.8 [d, $J_{CH} = 142.7$ Hz, $OCH(CH_3)_2$], 36.3 (t, $J_{CH} = 134.8$ Hz, C-2'), 24.2 and 24.0 [q, $J_{CH} = 134.4$ Hz, $OCH(CH_3)_2$], 20.9 (q, $J_{CH} = 130.1$ Hz, Ac), 17.4 (q, $J_{CH} = 128.1$ Hz, C-5'), 12.4 (q, $J_{CH} = 128.6$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 325.1400. Found 325.1421.

1-[3-O-Acetyl-2,5-dideoxy-4-(2-hydroxyethoxy)-α-L-lyxofuranosyl]thymine (**6a**) *and 1-[3-O-acetyl-2,5-deoxy-4-(2-hydroxyethoxy)-β-D-ribofuranosyl]thymine* (**6b**). A mixture of **1** (133 mg, 0.5 mmol), ethylene glycol (5 ml) and acetic acid (0.1 ml) in acetonitrile (20 ml) was boiled under reflux for 36 h, volatile matters were removed *in vacuo* by successive water- and oil-pump evacuation. The residue was separated on a silica gel column to give **6a** (70 mg, 43%) and **6b** (7 mg, 5%).

Compound **6a**: ^{1}H NMR ($CDCl_3$): 7.60 (d, 1 H, H-6), 6.63 (dd, $J_{1',2'} = 8.4$ Hz, $J_{1',2''} = 6.6$ Hz, 1 H, H-1'), 5.16 (d, $J_{2',3'} = 4.8$ Hz, 1 H, H-3'), 3.76 (m, 4 H, OCH_2CH_2OH), 2.42 (m, 2 H, H-2', H-2''), 2.17 (s, 3 H, Ac), 1.96 (d, 3 H, 5-CH_3), 1.47 (s, 3 H, H-5'). ^{13}C NMR ($CDCl_3$): 135.8 (d, $J_{CH} = 178.4$ Hz, C-6), 84.4 (d, $J_{CH} = 172.0$ Hz, C-1'), 77.6 (d, $J_{CH} = 161.8$ Hz, C-3'), 63.4 (t, $J_{CH} = 142.0$ Hz, OCH_2CH_2OH), 61.0 (t, $J_{CH} = 141.1$ Hz, OCH_2CH_2OH), 35.8 (t, $J_{CH} = 135.1$ Hz, C-2'), 20.8 (q, $J_{CH} = 126.2$ Hz, Ac), 16.7 (q, $J_{CH} = 128.0$ Hz, C-5'), 11.8 (q, $J_{CH} = 127.4$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 327.1192. Found 327.1175.

Compound **6b**: ^{1}H NMR ($CDCl_3$): 8.72 (br, 1 H, NH), 7.03 (d, 1 H, H-6), 6.25 (dd, $J_{1',2'} = 4.4$ Hz, $J_{1',2''} = 7.4$ Hz, 1 H, H-1'), 5.11 (t, $J_{2',3'} = 8.6$ Hz, 1 H, H-3'), 3.75 (m, 4 H, OCH_2CH_2OH), 2.52–2.42 (m, 2 H, H-2', H-2''), 2.14 (s, 3 H, Ac), 1.95 (d, 3 H, 5-CH_3), 1.59 (s, 3 H, H-5'). ^{13}C NMR ($CDCl_3$): 134.9 (d, $J_{CH} = 177.4$ Hz, C-6), 82.6 (d, $J_{CH} = 171.8$ Hz, C-1'), 75.7 (d, $J_{CH} = 147.3$ Hz, C-3'), 63.1 (t, $J_{CH} = 142.7$ Hz, OCH_2CH_2OH), 61.8 (t, $J_{CH} = 142.1$ Hz, OCH_2CH_2OH), 35.0 (t, $J_{CH} = 133.5$ Hz, C-2'),

20.8 (q, J_{CH} = 130.3 Hz, Ac), 20.1 (q, J_{CH} = 128.1 Hz, C-5′), 12.6 (q, J_{CH} = 130.7 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 327.1192. Found 327.1207.

1-[3-O-Acetyl-2,5-dideoxy-4-(1,2,4-triazol-1-yl)-α-L-lyxofuranosyl]thymine (**7a**) *and 1-[3-O-acetyl-2,5-dideoxy-4-(1,2,4-triazol-1-yl)-β-D-ribofuranosyl]thymine* (**7b**). A mixture of **1** (133 mg, 0.5 mmol), 1,2,4-triazole (345 mg, 5 mmol) and acetic acid (0.2 ml) in acetonitrile (20 ml) was boiled under reflux for 24 h and the solvent was then removed *in vacuo*. The residue was separated on a silica gel column to give **7a** (54 mg, 32%) and **7b** (39 mg, 23%).

Compound **7a**: ^{1}H NMR ($CDCl_3$): 8.26 [s, 1 H, H-3(triazole)], 8.02 [s, 1 H, H-5(triazole)], 7.13 (d, 1 H, H-6), 6.40 (t, $J_{1',2'}$ = 6.1 Hz, 1 H, H-1′), 5.76 (t, $J_{2',3'}$ = 7.9 Hz, 1 H, H-3′), 2.88 (dd, 2 H, H-2′ and H-2″), 2.11 (s, 3 H, Ac), 1.98 (d, 3 H, 5-CH_3), 1.85 (s, 3 H, H-5′). ^{13}C NMR ($CDCl_3$): 151.8 [d, J_{CH} = 207.8 Hz, C-3(triazole)], 141.7 [d, J_{CH} = 211.2 Hz, C-5(triazole)], 137.6 (d, J_{CH} = 178.5 Hz, C-6), 89.4 (d, J_{CH} = 168.5 Hz, C-1′), 76.1 (d, J_{CH} = 153.2 Hz, C-3′), 35.3 (t, J_{CH} = 136.5 Hz, C-2′), 23.5 (q, J_{CH} = 129.2 Hz, Ac), 20.2 (q, J_{CH} = 129.9 Hz, C-5′), 12.4 (q, J_{CH} = 129.6 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 334.1151. Found 334.1161.

Compound **7b**: ^{1}H NMR ($CDCl_3$): 9.86 (br, 1 H, NH), 8.41 [s, 1 H, H-3(triazole)], 8.08 [s, 1 H, H-5(triazole)], 7.31 (d, 1 H, H-6), 6.70 (dd, $J_{1',2'}$ = 9.5 Hz, $J_{1',2''}$ = 5.9 Hz, 1 H, H-1′), 5.82 (d, $J_{2',3'}$ = 5.9 Hz, 1 H, H-3′), 3.02 (ddd, J_{gem} = 14.4 Hz, 1 H, H-2′), 2.47 (dd, 1 H, H-2″), 2.21 (s, 3 H, Ac), 1.92 (s, 3 H, H-5′), 1.84 (d, 3 H, 5-CH_3). ^{13}C NMR ($CDCl_3$): 152.0 [d, J_{CH} = 208.9 Hz, C-3(triazole)], 141.7 [d, J_{CH} = 212.4 Hz, C-5(triazole)], 134.8 (d, J_{CH} = 184.2 Hz, C-6), 85.1 (d, J_{CH} = 170.8 Hz, C-1′), 77.2 (d, J_{CH} = 160.7 Hz, C-3′), 36.5 (t, J_{CH} = 135.7 Hz, C-2′), 20.8 and 20.6 (q, J_{CH} = 129.9 Hz, Ac and C-5′), 12.4 (q, J_{CH} = 129.2 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 334.1151. Found 334.1132.

1-(2,5-Dideoxy-4-methoxy-β-D-ribofuranosyl)thymine (**8b**). To a solution of **2** (90 mg, 0.4 mmol) in a mixture of methanol (5 ml) and benzene (10 ml) was added one drop of boron trifluoride–diethyl ether and the reaction was stirred at room temperature for 1 h. Then the reaction mixture was worked up and purified following the procedure described for **3a** and **3b** to give **8b** (69 mg, 68%). ^{1}H NMR ($CDCl_3$): 7.00 (d, 1 H, H-6), 6.13 (dd, $J_{1',2'}$ = 4.5 Hz, $J_{1',2''}$ = 7.2 Hz, 1 H, H-1′), 4.20 (dd, $J_{2',3'}$ = 9.2 Hz, $J_{2'',3'}$ = 8.3 Hz, 1 H, H-3′), 3.38 (s, 3 H, OCH_3), 2.35 (m, 2 H, H-2′, H-2″), 1.93 (d, 3 H, 5-CH_3), 1.54 (s, 3 H, H-5′). ^{13}C NMR ($CDCl_3$): 135.2 (d, J_{CH} = 177.4 Hz, C-6), 82.6 (d, J_{CH} = 171.8 Hz, C-1′), 75.5 (d, J_{CH} = 149.5 Hz, C-3′), 48.7 (q, J_{CH} = 143.8 Hz, OCH_3), 38.0 (t, J_{CH} = 134.3 Hz, C-2′), 18.1 (q, J_{CH} = 128.1 Hz, C-5′), 12.4 (q, J_{CH} = 128.0 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 255.0981. Found 255.0976.

1-(2,5-Dideoxy-4-ethoxy-β-D-ribofuranosyl)thymine (**9b**). To a solution of **2** (90 mg, 0.4 mmol) in a mixture of methanol (5 ml) and benzene (15 ml) was added one drop of boron trifluoride–diethyl ether and the reaction was stirred at room temperature for 1 h. Then the reaction mixture was worked up and purified following the procedure described for **3a** and **3b** to give **9b** (79 mg, 73%). ^{1}H NMR ($CDCl_3$): 9.41 (br, 1 H, NH), 6.99 (d, 1 H, H-6), 6.14 (dd, $J_{1',2'}$ = 4.6 Hz, $J_{1',2''}$ = 7.1 Hz, 1 H, H-1′), 4.16 (dd, $J_{2',3'}$ = 8.4 Hz, $J_{2'',3'}$ = 8.0 Hz, 1 H, H-3′), 3.67 (m, 2 H, OCH_2CH_3), 2.71 (d, J = 10.2 Hz, 1 H, 3′-OH), 2.33 (m, 2 H, H-2′, H-2″), 1.95 (d, 3 H, 5-CH_3), 1.56 (s, 3 H, H-5′), 1.24 (t, J = 7.1 Hz, 3 H, OCH_2CH_3). ^{13}C NMR ($CDCl_3$): 135.1 (d, J_{CH} = 182.0 Hz, C-6), 82.9 (d, J_{CH} = 171.9 Hz, C-1′), 75.7 (d, J_{CH} = 143.8 Hz, C-3′), 57.1 (t, J_{CH} = 142.7 Hz, OCH_2CH_3), 38.5 (t, J_{CH} = 134.3 Hz, C-2′), 19.3 (q, J_{CH} = 128.1 Hz, C-5′), 15.4 (q, J_{CH} = 125.8 Hz, OCH_2CH_3), 12.5 (q, J_{CH} = 129.2 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 269.1138. Found 269.1119.

1-(2,5-Dideoxy-4-isopropoxy-α-L-ribofuranosyl)thymine (**10a**) *and 1-(2,5-deoxy-4-isopropoxy-β-D-ribofuranosyl)-thymine* (**10b**). To a solution of **2** (90 mg, 0.4 mmol) in a mixture of isopropyl alcohol (2 ml) and acetonitrile (3 ml) was added one drop of boron trifluoride–diethyl ether and the reaction was stirred at room temperature for 1 h. Then the reaction mixture was concentrated to 5 ml. Toluene (3 × 20 ml) was added and the mixture was again concentrated to 5 ml. The residue was separated on a silica gel column to give **10a** (19 mg, 17%) and **10b** (33 mg, 29%).

Compound **10a**: ^{1}H NMR ($CDCl_3$): 9.33 (br, 1 H, NH), 7.70 (d, 1 H, H-6), 6.60 (t, $J_{1',2'}$ = 7.3 Hz, 1 H, H-1′), 4.11 [m, 2 H, $OCH(CH_3)_2$ and H-3′], 2.38 (dd, 2 H, H-2′, H-2″), 1.94 (s, 3 H, 5-CH_3), 1.57 (s, 3 H, H-5′), 1.23, 1.20 [2 × d, 6 H, $OCH_2CH_3)_2$]. ^{13}C NMR ($CDCl_3$): 136.7 (d, J_{CH} = 178.6 Hz, C-6), 84.8 (d, J_{CH} = 173.0 Hz, C-1′), 76.9 (d, J_{CH} = 152.7 Hz, C-3′), 66.4 [d, J_{CH} = 141.3 Hz, $OCH(CH_3)_2$], 38.7 (t, J_{CH} = 134.2 Hz, C-2′), 24.4 and 24.1 [q, J_{CH} = 124.9 Hz, $OCH(CH_3)_2$], 17.4 (q, J_{CH} = 128.1 Hz, C-5′), 12.3 (q, J_{CH} = 131.7 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 283.1294. Found 283.1294.

Compound **10b**: ^{1}H NMR ($CDCl_3$): 9.27 (br, 1 H, NH), 6.99 (d, 1 H, H-6), 6.15 (dd, $J_{1',2'}$ = 7.1 Hz, $J_{1',2''}$ = 5.0 Hz, 1 H, H-1′), 4.50–3.90 [m, 2 H, $OCH(CH_3)_2$ and H-3′], 2.83 (dd, 2 H, H-2′, H-2″), 1.95 (d, 3 H, 5-CH_3), 1.58 (s, 3 H, H-5′), 1.24, 1.20 [2 × d, 6 H, $OCH(CH_3)_2$]. ^{13}C NMR ($CDCl_3$): 135.1 (d, J_{CH} = 178.6 Hz, C-6), 83.1 (d, J_{CH} = 168.1 Hz, C-1′), 75.9 (d, J_{CH} = 151.2 Hz, C-3′), 65.4 [d, J_{CH} = 141.5 Hz, $OCH(CH_3)_2$], 38.7 (t, J_{CH} = 134.8 Hz, C-2′), 24.2 and 24.0 [q, J_{CH} = 131.3 Hz, $OCH(CH_3)_2$], 20.2 (q, J_{CH} = 129.1 Hz, C-5′), 12.5 (q, J_{CH} = 129.2 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 283.1294. Found 283.1292.

1-[2,5-Dideoxy-4-(1,2,4-triazol-1-yl)-α-L-ribofuranosyl]-thymine (**11a**) *and 1-[2,5-dideoxy-4-(1,2,4-triazol-1-yl)-β-D-ribofuranosyl]thymine* (**11b**). A mixture of **2** (90 mg, 0.4 mmol), 1,2,4-triazole (345 mg, 5 mmol) and acetic acid (0.2 ml) in acetonitrile (20 ml) was boiled under reflux for 24 h and the solvent was then evaporated and coevaporated with toluene to dryness. The residue was separated on a silica gel column to give **11a** (8 mg, 7%) and **11b** (53 mg, 45%).

Compound **11a**: ^{1}H NMR ($CDCl_3$–CD_3OD): 8.35 [s, 1 H, H-3(triazole)], 8.00 [s, 1 H, H-5(triazole)], 7.10 (d, 1 H, H-6), 6.31 (t, $J_{1',2'} = 6.2$ Hz, 1 H, H-1'), 4.70 (t, $J_{2',3'} = 7.5$ Hz, 1 H, H-3'), 2.58 (dd, 2 H, H-2', H-2''), 1.97 (s, 3 H, H-5'), 1.92 (d, 3 H, 5-CH_3). ^{13}C NMR ($CDCl_3$): 151.3 [d, $J_{CH} = 210.8$ Hz, C-3(triazole)], 141.4 [d, $J_{CH} = 211.9$ Hz, C-5(triazole)], 135.6 (d, $J_{CH} = 173.0$ Hz, C-6), 85.6 (d, $J_{CH} = 171.8$ Hz, C-1'), 75.6 (d, $J_{CH} = 159.5$ Hz, C-3'), 38.2 (t, $J_{CH} = 135.4$ Hz, C-2'), 20.8 (q, $J_{CH} = 129.9$ Hz, C-5'), 12.2 (q, $J_{CH} = 129.6$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 292.1046. Found 292.1049.

Compound **11b**: ^{1}H NMR ($CDCl_3$–CD_3OD): 8.45 [s, 1 H, H-3(triazole)], 8.04 [s, 1 H, H-5(triazole)], 7.37 (d, 1 H, H-6), 6.60 (dd, $J_{1',2'} = 8.4$ Hz, $J_{1',2''} = 6.0$ Hz, 1 H, H-1'), 4.75 (dd, $J_{2',3'} = 5.6$ Hz, $J_{2'',3'} = 2.3$ Hz, 1 H, H-3'), 2.80 (ddd, $J_{gem} = 13.7$, 1 H, H-2'), 2.44 (ddd, 1 H, H-2''), 1.93 (d, 3 H, 5-CH_3), 1.84 (s, 3 H, H-5'). ^{13}C NMR ($CDCl_3$): 150.8 [d, $J_{CH} = 211.8$ Hz, C-3(triazole)], 141.5 [d, $J_{CH} = 211.9$ Hz, C-5(triazole)], 134.8 (d, $J_{CH} = 184.2$ Hz, C-6), 87.9 (d, $J_{CH} = 170.8$ Hz, C-1'), 75.5 (d, $J_{CH} = 160.7$ Hz, C-3'), 36.9 (t, $J_{CH} = 135.7$ Hz, C-2'), 23.3 (q, $J_{CH} = 129.9$ Hz, C-5'), 12.1 (q, $J_{CH} = 129.2$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 292.1046. Found 292.1024.

General procedure for the removal of the 3'-O-acetyl group from **3a** *and* **4a**. Compounds **3a** and **4a** were treated with 32% aqueous ammonia (20 ml) at room temperature for 1 h and evaporated to dryness. The residue was purified on a silica gel column to give **8a** (92%) and **9a** (88%).

1-(2,5-Dideoxy-4-methoxy-α-L-ribofuranosyl)thymine (**8a**): ^{1}H NMR ($CDCl_3$): 7.36 (d, 1 H, H-6), 6.62 (t, $J_{1',2'} = 7.5$ Hz, 1 H, H-1'), 4.11 (t, $J_{2',3'} = 2.8$ Hz, 1 H, H-3'), 3.34 (s, 3 H, OCH_3), 2.35 (dd, 2 H, H-2', H-2''), 1.94 (d, 3 H, 5-CH_3), 1.48 (s, 3 H, H-5'). ^{13}C NMR ($CDCl_3$): 136.1 (d, $J_{CH} = 181.2$ Hz, C-6), 84.7 (d, $J_{CH} = 176.1$ Hz, C-1'), 76.2 (d, $J_{CH} = 159.2$ Hz, C-3'), 49.0 (q, $J_{CH} = 142.5$ Hz, OCH_3), 38.4 (t, $J_{CH} = 133.4$ Hz, C-2'), 15.3 (q, $J_{CH} = 127.8$ Hz, C-5'), 12.4 (q, $J_{CH} = 129.0$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 255.0981. Found 255.0980.

1-(2,5-Dideoxy-4-ethoxy-α-L-ribofuranosyl)thymine (**9a**): ^{1}H NMR ($CDCl_3$): 7.42 (d, 1 H, H-6), 6.63 (t, $J_{1',2'} = 7.5$ Hz, 1 H, H-1'), 4.14 (t, $J_{2',3'} = 2.7$ Hz, 1 H, H-3'), 3.61 (q, $J = 7.1$ Hz, 2 H, OCH_2CH_3), 2.38 (dd, 2 H, H-2', H-2''), 1.93 (d, 3 H, 5-CH_3), 1.51 (s, 3 H, H-5'), 1.23 (t, 3 H, OCH_2CH_3). ^{13}C NMR ($CDCl_3$): 136.0 (d, $J_{CH} = 183.1$ Hz, C-6), 84.8 (d, $J_{CH} = 171.9$ Hz, C-1'), 76.2 (d, $J_{CH} = 156.2$ Hz, C-3'), 57.1 (t, $J_{CH} = 143.1$ Hz, OCH_2CH_3), 38.4 (t, $J_{CH} = 133.7$ Hz, C-2'), 16.2 (q, $J_{CH} = 128.0$ Hz, C-5'), 15.1 (q, $J_{CH} = 125.8$ Hz, OCH_2CH_3), 12.2 (q, $J_{CH} = 129.2$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 269.1138. Found 269.1125.

1-(3-O-Acetyl-2-deoxy-4-methoxy-α-L-lyxofuranosyl)-thymine (**12a**) *and 1-(3-O-acetyl-2-deoxy-4-methoxy-β-D-ribofuranosyl)thymine* (**12b**). To a solution of **1** (133 mg, 0.5 mmol) in dry methanol (20 ml) was added *m*-chloroperbenzoic acid (121 mg, 0.7 mmol) and the solution was stirred for 4 h at room temperature. The reaction was quenched with aqueous ammonia and all volatile matter was removed by evaporation and coevaporation with toluene under vacuum to dryness. The residue was separated on a silica gel column to give **12a** (55 mg, 37%) and **12b** (39 mg, 26%).

Compound **12a**: ^{1}H NMR ($CDCl_3$–CD_3OD): 7.30 (d, 1 H, H-6), 6.64 (t, $J_{1',2'} = 7.4$ Hz, 1 H, H-1'), 5.29 (m, 1 H, H-3'), 3.88 (d, $J_{gem} = 12.5$ Hz, 1 H, H-5'), 3.60 (d, 1 H, H-5''), 3.42 (s, 3 H, CH_3O), 2.43 (m, 2 H, H-2' and H-2''), 2.17 (s, 3 H, Ac), 1.96 (d, 3 H, 5-CH_3). ^{13}C NMR ($CDCl_3$–CD_3OD): 135.1 (d, $J_{CH} = 181.3$ Hz, C-6), 84.4 (d, $J_{CH} = 169.2$ Hz, C-1'), 76.2 (d, $J_{CH} = 154.3$ Hz, C-3'), 56.4 (t, $J_{CH} = 143.9$ Hz, C-5'), 48.9 (q, $J_{CH} = 143.6$ Hz, CH_3O), 35.5 (t, $J_{CH} = 138.0$ Hz, C-2'), 20.7 (q, $J_{CH} = 129.8$ Hz, Ac), 12.4 (q, $J_{CH} = 129.2$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 313.1036. Found 313.1049.

Compound **12b**: ^{1}H NMR ($CDCl_3$–CD_3OD): 7.56 (d, 1 H, H-6), 6.31 (dd, $J_{1',2'} = 5.0$ Hz, $J_{1',2''} = 6.9$ Hz, 1 H, H-1'), 5.48 (t, $J_{2',3'} = 8.3$ Hz, 1 H, H-3'), 3.91 (d, $J_{gem} = 12.0$ Hz, 1 H, H-5'), 3.67 (d, 1 H, H-5''), 3.40 (s, 3 H, CH_3O), 2.51 (m, 2 H, H-2', H-2''), 2.15 (s, 3 H, Ac), 1.92 (d, 3 H, 5-CH_3). ^{13}C NMR ($CDCl_3$–CD_3OD): 135.6 (d, $J_{CH} = 182.0$ Hz, C-6), 83.0 (d, $J_{CH} = 171.9$ Hz, C-1'), 71.2 (d, $J_{CH} = 152.7$ Hz, C-3'), 60.6 (t, $J_{CH} = 143.8$ Hz, C-5'), 49.9 (q, $J_{CH} = 143.8$ Hz, CH_3O), 35.5 (t, $J_{CH} = 136.9$ Hz, C-2'), 20.6 (q, $J_{CH} = 130.2$ Hz, Ac), 12.4 (q, $J_{CH} = 129.2$ Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M - H^-$) 313.1036. Found 313.1016.

1-(2-Deoxy-4-methoxy-α-L-lyxofuranosyl)thymine (**13a**) *and 1-(2-deoxy-4-methoxy-β-D-ribofuranosyl)thymine* (**13b**). To a solution of **2** (112 mg, 0.5 mmol) in dry methanol (20 ml) was added *m*-chloroperbenzoic acid (121 mg, 0.7 mmol) and the solution was stirred for 4 h at room temperature. The reaction mixture was then worked up and purified following the procedure described for **12a** and **12b** to give **13a** (46 mg, 34%) and **13b** (36 mg, 26%).

Compound **13a**: ^{1}H NMR ($CDCl_3$–CD_3OD): 7.32 (d, 1 H, H-6), 6.65 (t, $J_{1',2'} = 7.6$ Hz, 1 H, H-1'), 4.32 (t, $J_{2',3'} = 3.1$ Hz, 1 H, H-3'), 3.84 (s, 2 H, H-5'), 3.34 (s, 3 H, CH_3O), 2.34 (dd, 2 H, H-2' and H-2''), 1.94 (d, 3 H, 5-CH_3). ^{13}C NMR ($CDCl_3$–CD_3OD): 135.6 (d, $J_{CH} = 181.3$ Hz, C-6), 85.2 (d, $J_{CH} = 170.6$ Hz, C-1'), 74.8 (d, $J_{CH} = 151.2$ Hz, C-3'), 56.6 (t, $J_{CH} = 144.0$ Hz, C-5'),

49.6 (q, J_{CH} = 143.7 Hz, CH_3O), 37.6 (t, J_{CH} = 137.5 Hz, C-2′), 12.3 (q, J_{CH} = 129.3 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M-H^-$) 271.0930. Found 271.0942.

Compound **13b**: ^{1}H NMR ($CDCl_3$–CD_3OD): 7.44 (d, 1 H, H-6), 6.20 (dd, $J_{1',2'}$ = 4.9 Hz, $J_{1',2''}$ = 6.6 Hz, 1 H, H-1′), 4.58 (t, $J_{2',3'}$ = 8.1 Hz, 1 H, H-3′), 3.91 (d, J_{gem} = 12.0 Hz, 1 H, H-5′), 3.73 (d, 1 H, H-5″), 3.42 (s, 3 H, CH_3O), 2.38 (m, 2 H, H-2′ and H-2″), 1.92 (d, 3 H, 5-CH_3). ^{13}C NMR ($CDCl_3$–CD_3OD): 136.0 (d, J_{CH} = 179.8 Hz, C-6), 83.7 (d, J_{CH} = 168.5 Hz, C-1′), 70.6 (d, J_{CH} = 147.2 Hz, C-3′), 59.6 (t, J_{CH} = 142.7 Hz, C-5′), 49.8 (q, J_{CH} = 143.8 Hz, CH_3O), 38.1 (t, J_{CH} = 134.8 Hz, C-2′), 12.3 (q, J_{CH} = 129.2 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M-H^-$) 271.0930. Found 271.0954.

1-(2-Deoxy-4-ethoxy-α-L-lyxofuranosyl)thymine (**14a**) *and 1-(2-deoxy-4-ethoxy-β-D-ribofuranosyl)thymine* (**14b**). To a solution of **2** (112 mg, 0.5 mmol) in dry ethanol (20 ml) was added *m*-chloroperbenzoic acid (121 mg, 0.7 mmol) and the solution was stirred for 4 h at room temperature. The reaction mixture was then worked up and purified following the procedure described for **12a** and **12b** to give **14a** (43 mg, 30%) and **14b** (38 mg, 27%).

Compound **14a**: ^{1}H NMR ($CDCl_3$–CD_3OD): 7.36 (d, 1 H, H-6), 6.64 (t, $J_{1',2'}$ = 7.5 Hz, 1 H, H-1′), 4.33 (t, $J_{2',3'}$ = 3.9 Hz, 1 H, H-3′), 3.86 (s, 2 H, H-5′), 3.70 (q, 3 H, CH_3CH_2O), 2.35 (dd, 2 H, H-2′ and H-2″), 1.95 (d, 3 H, 5-CH_3), 1.28 (t, 3 H, CH_3CH_2O). ^{13}C NMR ($CDCl_3$–CD_3OD): 135.6 (d, J_{CH} = 187.4 Hz, C-6), 85.2 (d, J_{CH} = 173.0 Hz, C-1′), 75.0 (d, J_{CH} = 156.2 Hz, C-3′), 57.5 (t, J_{CH} = 144.4 Hz, CH_3CH_2O), 56.9 (t, J_{CH} = 142.7 Hz, C-5′), 37.7 (t, J_{CH} = 134.2 Hz, C-2′), 14.8 (q, J_{CH} = 125.7 Hz, CH_3CH_2O), 12.1 (q, J_{CH} = 129.2 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M-H^-$) 285.1087. Found 285.1093.

Compound **14b**: ^{1}H NMR ($CDCl_3$–CD_3OD): 7.65 (d, 1 H, H-6), 6.23 (dd, $J_{1',2'}$ = 3.7 Hz, $J_{1',2''}$ = 7.3 Hz, 1 H, H-1′), 4.53 (t, $J_{2',3'}$ = 8.4 Hz, 1 H, H-3′), 3.90 (d, J_{gem} = 11.8 Hz, 1 H, H-5′), 3.67 (d, 1 H, H-5″), 3.66 (q, J = 7.0 Hz, 2 H, CH_3CH_2O), 2.35 (m, 2 H, H-2′ and H-2″), 1.89 (d, 3 H, 5-CH_3), 1.23 (t, 3 H, CH_3CH_2O). ^{13}C NMR ($CDCl_3$–CD_3OD): 136.3 (d, J_{CH} = 182.0 Hz, C-6), 83.3 (d, J_{CH} = 171.9 Hz, C-1′), 71.5 (d, J_{CH} = 152.7 Hz, C-3′), 60.3 (t, J_{CH} = 143.6 Hz, C-5′), 58.4 (t, J_{CH} = 143.0 Hz, CH_3CH_2O), 38.5 (t, J_{CH} = 136.9 Hz, C-2′), 15.2 (q, J_{CH} = 130.9 Hz, CH_3CH_2O), 12.6 (q, J_{CH} = 129.2 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M-H^-$) 285.1087. Found 285.1099.

1-(4-n-Butoxy-2-deoxy-α-L-lyxofuranosyl)thymine (**15a**) *and 1-(4-n-butoxy-2-deoxy-β-D-ribofuranosyl)thymine* (**15b**). Compound **2** (112 mg, 0.5 mmol) in a mixture of *n*-butyl alcohol (2 ml) and dichloromethane (20 ml) was heated to form a solution and cooled to room temperature. Then *m*-chloroperbenzoic acid (112 mg, 0.7 mmol) was added and the solution was stirred for 3 h at room temperature. The reaction mixture was then worked up and purified following the procedure described for **12a** and **12b** to give **15a** (33 mg, 21%) and **15b** (36 mg, 23%).

Compound **15a**: ^{1}H NMR ($CDCl_3$–CD_3OD): 7.38 (d, 1 H, H-6), 6.63 (t, $J_{1',2'}$ = 7.4 Hz, 1 H, H-1′), 4.34 (t, $J_{2',3'}$ = 3.1 Hz, 1 H, H-3′), 3.87 (s, 2 H, H-5′), 3.61 (m, 2 H, $CH_3CH_2CH_2CH_2O$), 2.35 (dd, 2 H, H-2′ and H-2″), 1.94 (d, 3 H, 5-CH_3), 1.52 (m, 4 H, $CH_3CH_2CH_2CH_2O$), 0.96 (t, J = 7.1 Hz, 3 H, $CH_3CH_2CH_2CH_2O$). ^{13}C NMR ($CDCl_3$–CD_3OD): 135.6 (d, J_{CH} = 177.5 Hz, C-6), 85.1 (d, J_{CH} = 173.0 Hz, C-1′), 74.8 (d, J_{CH} = 151.5 Hz, C-3′), 65.4 (t, J_{CH} = 141.6 Hz, $CH_3CH_2CH_2CH_2O$), 56.4 (t, J_{CH} = 144.2 Hz, C-5′), 37.7 (t, J_{CH} = 133.7 Hz, C-2′), 31.6 (t, J_{CH} = 125.0 Hz, $CH_3CH_2CH_2CH_2O$), 19.0 (t, J_{CH} = 126.4 Hz, $CH_3CH_2CH_2CH_2O$), 13.5 (q, J_{CH} = 124.7 Hz, $CH_3CH_2CH_2CH_2O$), 11.9 (q, J_{CH} = 129.2 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M-H^-$) 313.1400. Found 313.1395.

Compound **15b**: ^{1}H NMR ($CDCl_3$): 9.44 (br, 1 H, NH), 7.35 (d, 1 H, H-6), 6.18 (t, $J_{1',2'}$ = 6.8 Hz, 1 H, H-1′), 4.61 (t, $J_{2',3'}$ = 7.7 Hz, 1 H, H-3′), 3.93 (d, J_{gem} = 12.3 Hz, 1 H, H-5′), 3.77 (d, 1 H, H-5″), 3.65 (m, 2 H, $CH_3CH_2CH_2CH_2O$), 2.41 (dd, 2 H, H-2′ and H-2″), 1.90 (d, 3 H, 5-CH_3), 1.49 (m, 4 H, $CH_3CH_2CH_2CH_2O$), 0.93 (t, J = 7.3 Hz, 3 H, $CH_3CH_2CH_2CH_2O$). ^{13}C NMR ($CDCl_3$): 136.2 (d, J_{CH} = 179.7 Hz, C-6), 84.3 (d, J_{CH} = 170.8 Hz, C-1′), 70.8 (d, J_{CH} = 147.2 Hz, C-3′), 62.2 (t, J_{CH} = 143.2 Hz, $CH_3CH_2CH_2CH_2O$), 60.5 (t, J_{CH} = 143.8 Hz, C-5′), 38.4 (t, J_{CH} = 135.4 Hz, C-2′), 31.9 (t, J_{CH} = 125.6 Hz, $CH_3CH_2CH_2CH_2O$), 19.1 (t, J_{CH} = 126.9 Hz, $CH_3CH_2CH_2CH_2O$), 13.7 (q, J_{CH} = 133.7 Hz, $CH_3CH_2CH_2CH_2O$), 12.4 (q, J_{CH} = 129.2 Hz, 5-CH_3). MS (FAB$^-$): Calc. for ($M-H^-$) 313.1400. Found 313.1427.

2′,5′-Dideoxy-4′-hydroxy-3′,4′-O-[(R)-1-isopropoxyethylidene]thymidine (**16**). Compound **1** (133 mg, 0.5 mmol) in a mixture of isopropyl alcohol (4 ml) and dichloromethane (20 ml) was heated to form a solution and cooled to room temperature. *m*-Chloroperbenzoic acid (121 mg, 0.7 mmol) was then added and the solution was stirred for 5 h at room temperature. Then the reaction mixture was worked up and purified following the procedure described for **12a** and **12b** to give **16** (51 mg, 30%). ^{1}H NMR ($CDCl_3$–CD_3OD): 7.61 (d, 1 H, H-6), 6.42 (dd, $J_{1',2'}$ = 9.4 Hz, $J_{1',2''}$ = 5.0 Hz, 1 H, H-1′), 4.87 (d, $J_{2',3'}$ = 4.7 Hz, 1 H, H-3′), 3.92 [m, 1 H, $CH(CH_3)_2$], 3.90 (s, 2 H, H-5′), 2.53 (dd, J_{gem} = 13.8 Hz, 1 H, H-2″), 2.15 (m, 1 H, H-2′), 1.90 (d, 3 H, 5-CH_3), 1.68 (s, 3 H, CH_3CO_3), 1.18 [d, J = 6.1 Hz, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$–CD_3OD): 135.9 (d, J_{CH} = 183.1 Hz, C-6), 84.9 (d, J_{CH} = 170.8 Hz, C-1′), 81.0 (d, J_{CH} = 161.8 Hz, C-3′), 66.2 [d, J_{CH} = 141.6 Hz, $CH(CH_3)_2$], 63.0 (t, J_{CH} = 143.8 Hz, C-5′), 37.7 (t, J_{CH} = 134.3 Hz, C-2′), 23.4 [q, J_{CH} = 126.9 Hz, $(CH_3)_2C$], 22.8 (q, J_{CH} = 128.0 Hz, CH_3CO_3), 12.0 (q, J_{CH} = 129.2 Hz, 5-CH_3). MS (FAB$^-$): Calc. for (M − H$^-$) 341.1349. Found 341.1325.

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