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N.m.r. studies of the conformation of analogues of methyl β-lactoside in methyl sulfoxide-d_6

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ABSTRACT

The ^{1}H- and ^{13}C-n.m.r. spectra of solutions of methyl β-lactoside (**1**), all of its monodeoxy derivatives (**2**, **3**, **6**–**10**), the 3-*O*-methyl derivative (**4**), and methyl 4-*O*-β-D-galactopyranosyl-D-xylopyranoside (**5**) in methyl sulfoxide-d_6 have been analysed. The n.O.e.'s and specific deshieldings indicate similar distributions of low-energy conformers, comparable to those in aqueous solution. The major conformer has torsion angles ϕ_H and ψ_H of 49° and 5°, respectively, with contributions of conformers with ϕ/ψ 24°/−59°, 22°/32°, and 6°/44°.

INTRODUCTION

We have reported[1,2] on the recognition of methyl β-lactoside (**1**) and some of its derivatives by the β-galactoside-specific lectins ricin (RCA 60) and agglutinin (RCA 120), isolated from the seeds of the castor plant *Ricinus communis*. Compound **1**, methyl 2- (**2**), 3- (**3**), 6- (**6**), 2′- (**7**), 3′- (**8**), 4′- (**9**), and 6′-deoxy-β-lactoside (**10**), methyl 3-*O*-methyl-β-lactoside (**4**), methyl 4-*O*-β-D-galactopyranosyl-D-xylopyranoside (**5**), lactal (**11**), and 1,6-anhydrolactose (**12**) were used to probe the combining sites of these lectins. The distribution of low-energy conformers of **1**–**12**, predicted[1,2,4,5] by hard sphere exo-anomeric (HSEA) calculations followed by a full optimisation of the local minima of the HSEA map using the MM2 programme[6], was supported by the n.m.r. data[1,2,4,5] for solutions in D_2O. It was assumed[7] that, when bound to the lectins, the disaccharide derivatives had a distribution of low-energy conformers similar to those in aqueous solution. Thus, the observed dissociation constants could be correlated with individual functional groups of the carbohydrate derivatives[1,2]. This assumption accords with the observation[8] that the conformations around the glycosidic bonds are determined mainly by steric interactions and should be relatively insensitive to the polarity of the medium. However, a non-polar medium could induce the formation of intramolecular hydrogen bonds and cause local changes in conformation[9]. A recent study[10] of the conformation of **1** bound to ricin, using n.O.e. data and selective deuteration, indicated that the changes in conformation on binding are small but significant and that, probably, only one conformer is involved in the formation of the complex.

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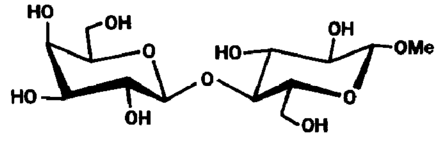

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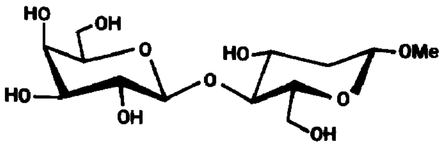

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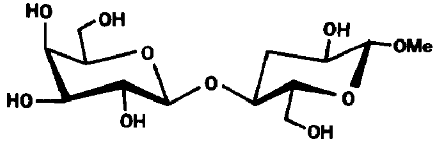

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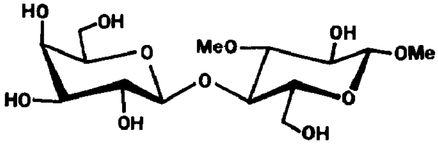

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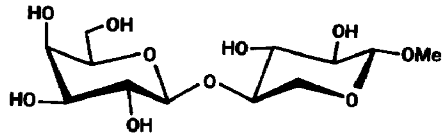

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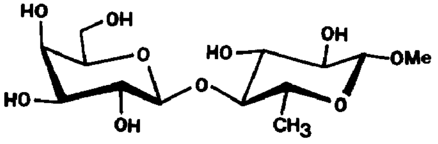

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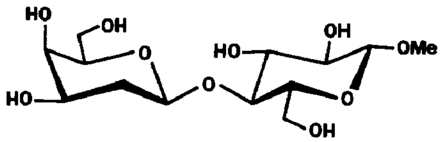

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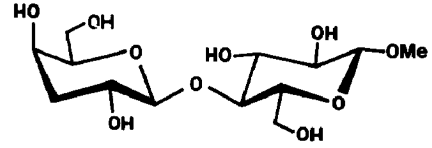

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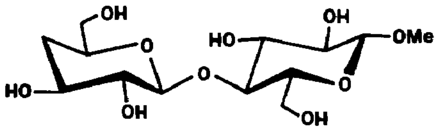

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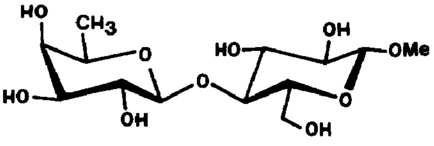

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Enzymes and membranes tend to be lipophilic[11–15] and such solvents as methyl sulfoxide may provide a better model for the study of specific interactions[16]. We now report on an assessment of the conformations of **1**–**10** in methyl sulfoxide-d_6, using n.m.r. spectroscopy, and a comparison with those in solution in D_2O.

EXPERIMENTAL

Molecular mechanics calculations. — HSEA energy calculations were performed as described[1]. After the lone pairs were added to the oxygen atoms, the local minima of the energy map obtained were optimised through molecular mechanics, using the MM2(85) program[6] with a value for the dielectric constant (ε) of 1.

N.m.r. spectroscopy. — ^{1}H-N.m.r. spectra (300 MHz) were obtained with a Varian XL-300 spectrometer. Solutions of samples (20 mg) in 99.98% $(CD_3)_2SO$ (0.5 mL) were degassed in the n.m.r. tube under argon. Chemical shifts (δ, p.p.m.) were measured at 30° by reference to residual Me_2SO (2.49 p.p.m.). Double-quantum-filtered phase-sensitive COSY experiments were performed using the pulse sequence 90°–t_1–90°–acq. A 512 × 1K data matrix was obtained, which was zero-filled prior to Fourier transformation. 1D-N.O.e. experiments were performed under steady-state conditions through the interleaved differential technique; 512 f.i.d.'s were accumulated for each irradiation. 2D-NOESY experiments were performed in the phase-sensitive mode with the pulse sequence 90°–t_1–90°–t_m–acq, a mixing time of 0.5 s, and relaxation delay of 3 s. The cross-peak and diagonal-peak volumes were obtained using standard Varian software. The estimated error was 10%. Interatomic distances were estimated[17] from n.O.e. ratios. From the n.O.e. values for a pair of protons at a known fixed distance, the n.O.e. value for a given proton can be translated in terms of the average distance $<r^{-6}>^{-1/6}$. When these distances were compared with the $<r^{-6}>^{-1/6}$ and $(<r^{-3}>^2)^{-1/6}$ distances expected for a Boltzman distribution of the low-energy conformers calculated using molecular mechanics[18], similar results were obtained.

^{13}C-N.m.r. spectra (50 MHz) were obtained with a Bruker AM-200 spectrometer equipped with a dual probe. Chemical shifts are expressed in p.p.m. relative to external acetone at δ 31.5. Spin–lattice relaxation times were determined by the inversion–recovery technique, using a non-linear least-squares procedure. Two independent sets of 8 delays were used in each determination. Heteronuclear correlation experiments with F1-decoupling were performed using standard Bruker software. A 64 × 4K data matrix was obtained and processed after zero-filling.

Compounds **1–10** were synthesised as described[2].

RESULTS AND DISCUSSION

The values of the steric energy differences for the different conformers of **1**, **3**–**5**, and **7** have been calculated[1]. Four local minima (A–C and C′), out of the six (A–E and C′) obtained for **1** at a level of relative steric energy of 4 kcal/mol (Table IX), are included in a region with $\Delta E < 1$ kcal/mol which describes ~5% of the complete ϕ,ψ energy surface. One of these conformers (A, ϕ_H/ψ_H 49°/5°) had a geometry similar to those found in the crystalline state for β-lactose[19], lactose $CaBr_2 \cdot H_2O$[20], and β-cellobiose[21], and a second minimum (B, ϕ_H/ψ_H 24°/−59°) corresponded to the crystalline structure of methyl β-cellobioside[22]. Solid-state structures similar to those of the remaining minima (C, ϕ_H/ψ_H −22°/−32°, C′, ϕ_H/ψ_H 6°/−44°, D, ϕ_H/ψ_H 27°/176°, and E,

ϕ_H/ψ_H 175°/−2°) have not yet been reported for β-(1→4)-linked disaccharides. A similar, most probable set of ϕ_H/ψ_H angles has been calculated for the lactose fragment of globoside, using the MM-2 programme[23]. The ^{1}H- and ^{13}C-n.m.r. data determined for solutions in D_2O indicated a similar distribution of low-energy conformers for **1**–**10**, which may be described by conformer A with smaller contributions of conformers B, C, and C′. The relevant interatomic distances of these major conformers for **1** and **3**–**7** are given in Table I. It was assumed that deoxygenation at positions 2, 3′, 4′, and 6′ (**2**, **8**, **9**, and **10**, respectively) would produce minor changes in the conformation around the glycosidic bond.

TABLE I

Interatomic distances (<4.5 Å) for the major conformers of **1** and **3**–**7**, as obtained by MM2 calculations

Atom pair	*Interatomic distance for conformer*			
	A	*B*	*C*	*C′*
H-1′–H-4	2.30	2.33	2.27	2.23
H-1′–H-3	–	3.44/2.48[a]	3.60/2.36[a]	3.50/2.38[a]
H-1′–H-6a	2.74[b,c]	–	–	–
H-1′–H-6b	2.58[b]	–	–	–
H-1′–H-5*eq*	2.93[d]	–	–	–
H-1′–O-6	2.76[c]	–	–	–
H-1′–O-3	4.16	2.48	2.45	2.47
H-6a–O-2′	2.96[b]	3.78[c]	3.00[b]	3.53[c]
H-6b–O-2′	2.99	3.64	3.12[b]	–
O-3–O-5′	2.88	2.89	3.50	3.06

[a] H-3*eq* of **3**; [b] *gauche–trans* orientation; [c] *gauche–gauche* orientation; [d] H-5*eq* of **5**.

The chemical shift data for solutions of **1**–**10** in $(CD_3)_2SO$ are given in Table II and the $^3J_{H,H}$ values are given in Table III. The J values indicated that all of the pyranoid rings adopted $^4C_1$ conformations. The $J_{5,6a}$ and $J_{5,6b}$ values indicated an ~1:1 equilibrium between the *gt* and *gg* rotamers as reported for β-D-glucopyranosides[24], whereas the values of $J_{5',6'a}$ and $J_{5',6'b}$ indicated a preponderance of the *gt* rotamer in agreement with reported data[1,25–27]. The ^{1}H chemical shifts (Table II) do not show significant differences among the different compounds, apart from those to be expected by changes in structure. However, the deshielding of H-1′ in **4** may indicate its proximity to O-6. Likewise, the deshielding of H-5′ in **5** and **6**, and the shielding of H-5,6a,6b in **7**, could indicate the proximity of C-5,6 of the D-glucopyranoid ring and the C-2′ region. As discussed[1], conformer A has O-6 in close proximity to H-1′ in the *gg* rotamer, and O-2′ to H-6a in the *gg* rotamer and to H-6b in the *gt* rotamer (Table I). Therefore, these chemical shift data indicate the preponderance of conformer A in solutions in $(CD_3)_2SO$.

The ^{13}C-n.m.r. data in Table IV for solutions of **1**–**10** in $(CD_3)_2SO$ show that C-1′ is deshielded in **3** and that C-2′,5′ are shielded in **5**. These effects are also consistent with a

TABLE II

^{1}H-N.m.r. chemical shifts[a] (δ, p.p.m.) for methyl β-lactoside (**1**) and its derivatives (**2–10**) in solution in $(CD_3)_2SO$ at 30°

Compound	*Unit*	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6a*	*H-6b*
1	Gal	4.19	3.32	3.30	3.62	3.30	3.52	3.46
	Glc	4.09	3.00	3.32	3.44	3.38	3.74	3.61
2	Gal	4.18	3.30	3.30	3.60	n.d.[b]	3.50	3.44
	Glc	4.40	2.02 1.25	3.53	3.21	n.d.	3.76	3.61
3	Gal	4.15	3.22	3.23	3.60	3.31	~3.45	
	Glc	4.07	3.15	2.30 1.37	3.41	3.37	3.71	3.56
4	Gal	4.29	3.26	3.26	3.63	3.31	3.55	3.45
	Glc	4.07	3.05	3.10	3.49	3.22	3.72	3.65
5	Gal	4.20	3.35	3.28	3.61	3.38	~3.50	
	Xyl	4.03	2.99	3.25	3.50	3.15 3.86	–	–
6	Gal	4.18	3.32	3.29	3.61	3.35	3.50	3.45
	Glc	4.08	3.01	3.24	2.96	3.09	1.26	–
7	Gal	4.46	1.71 1.59	3.52	n.d.	3.31	n.d.	n.d.
	Glc	4.08	2.98	3.28	n.d.	3.24	3.60	3.48
8	Gal	4.18	3.53	1.95 1.47	3.67	n.d.	3.50	3.41
	Glc	4.09	3.00	3.29	3.51	n.d.	3.74	3.65
9	Gal	4.20	2.90	3.40	1.76 1.18	3.43	3.40	3.33
	Glc	4.09	2.99	3.29	3.48	3.38	3.74	3.60
10	Gal	4.20	3.29	n.d.	3.40	3.63	1.12	–
	Glc	4.09	3.00	3.26	3.43	3.35	3.73	3.58

[a] Reference to Me_2SO at 2.49 p.p.m. [b] Not determined.

preponderance of conformer A. The shielding of C-2 and the deshielding of C-4 in **4** can be accounted for by the influence of the MeO-3. The shielding of C-4 in **7** cannot be explained easily.

The influence of the solvent on the ^{13}C chemical shifts is shown in Table V. The major differences are found for C-4. The differences for C-2 in **4** and **5** show a different sign, which may reflect small changes in solvation or conformation.

The ^{1}H chemical shifts for the hydroxylic protons at 30° and the differences between these values and those determined at 70° are given in Table VI. These differ-

TABLE III

$J_{H,H}$ Values (Hz) for **1**–**10** in solution in $(CD_3)_2SO$ at 30°

Compound	*Unit*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
1	Gal	7.9	n.d.[a]	3.5	0.6	4.0	8.2	−12.0
	Glc	7.8	9.9	9.9	9.2	2.2	5.1	−12.1
2	Gal	7.9	9.9	3.6	0.9	n.d.	n.d.	n.d.
	Glc	9.9	12.1,5.1	9.2	n.d.	1.6	n.d.	−12.1
		1.9	−12.4[b]					
3	Gal	8.0	10.0	3.5	0.9	4.3	7.4	n.d.
	Glc	8.1	11.6	11.7,5.0	9.9	2.3	5.8	−12.2
			4.9	−11.9[b]				
4	Gal	7.7	10.5	4.1	0.9	4.4	7.5	−11.5
	Glc	8.1	n.d.	n.d.	9.5	2.2	5.2	−12.4
5	Gal	7.7	10.0	3.6	0.9	n.d.	n.d.	n.d.
	Xyl	7.9	9.4	9.1	5.3,10.4.11.5[b]			
6	Gal	8.1	9.9	3.5	1.0	3.8	8.4	−11.6
	Glc	8.1	9.3	9.4	9.5	6.4	–	–
7	Gal	9.8	4.8,12.1	3.2	0.9	4.3	7.8	n.d.
		2.2	−12.1[b]					
	Glc	7.9	8.5	9.4	n.d.	2.1	5.1	−12.1
8	Gal	7.9	12.1	3.1,2.9	0.9	n.d.	n.d.	n.d.
			5.2	−13.5[b]				
	Glc	8.0	9.2	10.0	9.0	1.8	4.7	−12.1
9	Gal	7.3	9.2	11.9	11.9,1.9	n.d.	n.d.	n.d.
				5.1	−12.5[b]			
	Glc	7.2	9.3	9.4	9.5	0.9	4.5	−12.1
10	Gal	7.9	10.0	3.5	0.8	6.5	–	–
	Glc	7.9	8.6	n.d.	n.d.	1.4	4.3	−12.2

[a] Not determined. [b] Geminal coupling.

ences are smaller for HO-3 than for any other hydroxyl group in the compounds studied with the exception of **5**. The $J_{HO\text{-}3,H\text{-}3}$ values were < 2 Hz, but the value (4–7 Hz) for **5** was similar to those observed for the remaining HO–H couplings. Thus, HO-3 may participate in inter-ring hydrogen bonding, probably with O-5′, as occurs in the crystal of β-lactose[19]. Either conformer A or B would permit the formation of this hydrogen bonding. The exceptional behavior of HO-3 in **5**, which shows a $\Delta\delta$ value similar to that of the other hydroxylic protons in the molecule, accords with observations on xylans[28].

The ^{13}C relaxation times for **1** at different temperatures are given in Table VII. The T_1 values are similar and, therefore, the molecule does not have a preferred axis of rotation. The relaxation times of C-6 and C-6′ reflect an additional degree of freedom

TABLE IV

^{13}C-N.m.r. chemical shifts[a] (δ, p.p.m.) for methyl β-lactoside (**1**) and its derivatives (**2**–**10**) in solution in $(CD_3)_2SO$ at 30°

Compound	*Unit*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*OCH_3*
1	Gal	105.7	72.4	75.0	70.0	77.4	62.4	–
	Glc	105.5	75.1	76.7	82.5	76.8	62.3	56.9
2	Gal	105.7	72.4	75.0	69.9	77.3	62.1	–
	Glc	101.9	40.0	70.7	84.2	76.8	62.5	57.5
3	Gal	106.2	72.5	75.1	69.8	76.9	62.2	–
	Glc	107.7	69.1	40.8	80.6	75.5	62.4	57.6
4	Gal	105.2	73.3	75.2	69.6	77.0	62.0	–
	Glc	105.4	74.8	86.7	78.1	76.9	61.9	57.6
5	Gal	106.2	71.6	74.8	69.9	77.3	62.2	–
	Xyl	104.0	74.8	76.3	77.9	65.2	–	57.7
6	Gal	105.9	72.2	75.0	69.8	77.2	62.0	–
	Glc	105.1	75.0	76.4	87.7	71.6	19.2	57.7
7	Gal	102.3	36.5	69.5	68.1	77.6	62.4	–
	Glc	105.4	74.9	76.5	81.6	76.5	61.9	57.7
8	Gal	107.2	66.4	40.5	66.3	80.5	63.4	–
	Glc	105.1	74.9	76.6	82.2	76.7	62.3	57.6
9	Gal	105.4	72.1	74.4	37.2	76.6	65.3	–
	Glc	105.3	74.9	76.7	82.4	77.1	62.9	57.6
10	Gal	105.3	72.5	74.9	72.3	72.0	18.3	–
	Glc	105.2	75.1	76.2	81.8	76.5	62.0	57.5

[a] Reference to external acetone at 31.5 p.p.m.

due to the rotation of the hydroxymethyl groups. The range of τ_c indicates that **1** is close to the extreme narrowing limit at 300 MHz in $(CD_3)_2SO$ between 30° and 70°, and that the n.O.e. data can be used to analyse the conformations of **1** and, most likely, of its analogues **2**–**10**, in this solvent.

As with solutions of these compounds in D_2O[1], both 1D-n.O.e. and 2D-NOESY experiments showed that the n.O.e. ratio H-1′–H-4/H-1′–H-3′ (H-5′) was approximately constant for all of the compounds studied and indicated similar conformations. The observed n.O.e.'s for solutions in $(CD_3)_2SO$ and the corresponding internuclear distances are given in Table VIII. The deuterated derivative of **1** was used in order to reduce major diffusion pathways and simplify the spectrum[10]. The existence of n.O.e.'s between H-1′ and H-4 but not between H-1′ and H-3 or H-5, or between H-2′ and H-4, indicated higher proportions of conformers A, B, and/or C. An important contribution of conformer A can be deduced from the observed n.O.e. between H-1′ and H-5*eq* in **5** and

TABLE V

^{13}C-N.m.r. chemical shift differences[a] (δ, p.p.m.) for solutions in $(CD_3)_2SO$ and D_2O[b] of methyl β-lactoside (**1**) and its derivatives (**2**–**10**) at 30°

Compound	*Unit*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*OCH_3*
1	Gal	1.3	0.2	1.1	0.2	0.8	0.1	–
	Glc	1.2	1.0	0.9	2.6	0.7	0.9	−0.5
2	Gal	1.3	0.1	1.1	0.1	0.7	−0.1	–
	Glc	0.1	1.5	0.2	2.7	0.7	0.8	−0.3
3	Gal	1.2	0.4	1.1	0.0	0.6	0.1	–
	Glc	1.2	0.3	2.1	1.0	0.4	0.5	−0.5
4	Gal	1.1	0.7	1.3	−0.3	0.6	−0.3	–
	Glc	1.1	1.4	1.9	1.4	0.5	0.7	−0.6
5	Gal	1.1	−0.3	0.9	0.0	0.7	−0.2	–
	Xyl	0.9	0.7	1.1	0.1	1.1	–	−0.7
6	Gal	1.4	0.1	1.1	−0.1	0.6	−0.3	–
	Glc	0.8	0.7	0.8	2.6	−0.7	1.3	−0.7
7	Gal	0.8	1.9	0.7	0.3	0.8	−0.2	–
	Glc	1.1	0.9	1.0	2.1	0.7	0.5	−0.7
8	Gal	1.1	−0.4	2.3	−0.4	0.9	1.0	–
	Glc	0.8	0.9	1.0	2.4	0.7	1.0	−0.8
9	Gal	1.2	0.8	0.4	2.1	1.0	0.7	–
	Glc	1.1	0.9	0.8	2.2	1.0	0.9	−0.7
10	Gal	1.1	0.2	1.1	0.2	0.2	1.8	–
	Glc	1.1	1.2	0.7	1.8	0.7	0.8	−0.8
11	Gal	1.2	0.3	1.1	0.0	0.5	0.1	−0.7

[a] Reference to external acetone at 31.5 p.p.m. [b] A positive number indicates relative deshielding in $(CD_3)_2SO$.

between H-1′ and Me-5 in **6**. Selective, ω_1-decoupled 2D-ROESY experiments indicated[23] that, according to the observed n.O.e. contact between HO-2′ and HO-3, the lactose moiety of globoside in solution in $(CD_3)_2SO$ may adopt a conformation in which either ϕ_H or ψ_H is close to 180° (*i.e.*, conformers E or D, respectively) and may indicate a pronounced flexibility of this linkage. We have not observed, however, the n.O.e.'s expected for these conformers between H-2′–H-4, H-1′–H-3, and H-1′–H-5. In accordance with these results, it was not possible, in the study referred to above[23], to corroborate the presence of conformers D and E by n.O.e.'s referring to unexchangeable C-linked protons.

Thus, the distribution of low-energy conformers is similar in **1**–**10** and close to that determined by MM-2 calculations and n.m.r. spectroscopy on solutions in D_2O.

TABLE VI

^{1}H-N.m.r. chemical shifts at 30° (δ, p.p.m.) and chemical shift differences[a] ($\Delta\delta$) between 30° and 70° for the hydroxylic protons of **1**–**11** for solutions in $(CD_3)_2SO$

Compound		*OH-2*	*OH-3*	*OH-6*	*OH-2'*	*OH-3'*	*OH-4'*	*OH-6'*
1	δ	5.12	4.63	4.53	5.04	4.73	4.46	4.61
	$\Delta\delta$	0.27	0.08	0.21	0.21	0.26	0.21	0.18
2	δ	–	4.64	4.51	5.04	4.73	4.46	4.62
	$\Delta\delta$	–	0.08	0.21	0.19	0.23	0.20	0.18
3	δ	4.96	–	4.47	4.86	4.64	4.32	4.51
	$\Delta\delta$	0.23	–	0.22	0.23	0.25	0.21	0.19
4	δ	5.21	–	4.45	4.93	4.64	4.31	4.66
	$\Delta\delta$	0.30	–	0.26	0.29	0.26	0.27	0.28
5	δ	5.13	4.98	–	4.78	4.69	4.39	4.58
	$\Delta\delta$	0.34	0.28	–	0.25	0.31	0.26	0.24
6	δ	5.11	4.64	–	5.00	~4.60	4.44	~4.60
	$\Delta\delta$	0.28	0.09	–	0.22	b.s.[b]	b.s.	b.s.
7	δ	5.10	4.69	4.62	–	4.68	4.35	4.65
	$\Delta\delta$	0.27	0.12	0.21	–	0.27	0.24	0.23
8	δ	5.13	4.70	4.56	4.99	–	4.64	4.63
	$\Delta\delta$	0.26	0.08	0.21	0.19	–	0.18	0.19
9	δ	5.11	4.65	4.56	5.18	4.90	–	4.73
	$\Delta\delta$	0.23	0.08	0.20	0.32	0.21	–	0.19
10	δ	5.12	4.60	4.51	5.04	4.69	4.52	–
	$\Delta\delta$	0.25	0.08	0.20	0.20	0.24	0.22	–
11	δ	–	–	–	4.82	4.62	4.28	4.52
	$\Delta\delta$	–	–	–	0.26	0.26	0.21	0.20

[a] Reference to Me_2SO at 2.49 p.p.m. [b] Broad signal at 70°.

The less polar aprotic medium does not influence significantly the conformational equilibrium, which may be described by conformer A with contributions of conformers B and C/C'.

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TABLE VII

^{13}C-N.m.r. relaxation times[a] and estimated average correlation times for **1** in solution in $(CD_3)_2SO$ at different temperatures

Atom	*30°*	*40°*	*50°*	*60°*	*70°*
C-1	0.27	0.31	0.38	0.51	0.68
C-2	0.24	0.31	0.40	0.53	0.65
C-3	0.24	0.27	0.37	0.50	0.64
C-4	0.28	0.33	0.39	0.54	0.65
C-5	0.25	0.27	0.37	0.50	0.64
C-6	0.22	0.26	0.35	0.49	0.62
C-1′	0.23	0.27	0.37	0.50	0.68
C-2′	0.23	0.29	0.40	0.45	0.61
C-3′	0.25	0.32	0.41	0.53	0.69
C-4′	0.23	0.27	0.31	0.45	0.61
C-5′	0.24	0.27	0.37	0.41	0.58
C-6′	0.16	0.19	0.23	0.27	0.33
τ_c (ns)	0.20	0.15	0.12	0.10	0.08

[a] Maximum estimated error is ±10%.

TABLE VIII

N.O.e.'s (%) and corresponding internuclear distances for selected protons of **1** and **3–6** in solution in $(CD_3)_2SO$ (irradiated proton in parentheses[a])

	1[b,c]		**3**[c]		**4**		**5**[c]		**6**	
	N.O.e. (%)	r (*Å*)	*N.O.e.* (%)	r (*Å*)	*N.O.e.* (%)	r (*Å*)	*N.O.e.* (%)	r (*Å*)	*N.O.e.* (%)	r (*Å*)
H-3′–{H-1′}	–	2.5	[d]	2.5	14.0[e]	2.5	6.7[e]	2.5	[d]	2.5
							9.0[f]	2.5		
H-5′–{H-1′}	10.0[e]	2.5	15.0[f]	2.5	15.0[f]	2.5	7.5[e]	2.5	[d]	2.5
							11.0[f]	2.5		
H-4–{H-1′}	13.0[e]	2.4	12.0[e]	–	13.0[e]	2.5	6.1[e]	2.6	10.0[e]	–
			18.0[f]	2.6	15.0[f]	2.7	9.5[f]	2.5–2.6		
H-6–{H-1′}	N.o.[g]		N.o.		N.o.		1.6[e,h]	2.8–2.9	2.0[e]	
							1.5[f,h]	2.8–3.1		
H-1′–{H-6}	–		–		–		–		2.0[e]	3.1
H-4–{H-6}	–		–		–		–		7.0[e]	
H-5–{H-6}	–		–		–		–		10.0[e]	

[a] Estimated error ±10%. [b] Deuterated analog (see text). [c] Also NOESY. [d] Obscured by residual water. [e] At 30°. [f] At 50°. [g] Not observed. [h] H-5*eq*–{H-1′}.

TABLE IX

Relative steric energy values and estimated populations at 30° of the stable conformers of **1**, calculated by the MM2 program

Conformer (ϕ/ψ)	*Relative steric energy (kcal/mol)*							
	Rotamer							
	gg/gt		gg/tg		gt/gt		gt/tg	
	ΔE	*Pop* (%)	ΔE	*Pop* (%)	ΔE	*Pop* (%)	ΔE	*Pop* (%)
A (49°/5°)	0.00	18.9	1.49	1.5	0.19	13.7	1.76	1.0
B (24°/−59°)	0.09	16.2	1.31	2.1	0.12	15.4	1.17	2.6
C (−22°/−32°)[a]	–	–	–	–	0.65	6.3	1.71	1.1
C′ (6°/−44°)[b]	0.07	17.0	1.29	2.2	–	–	–	–
D (27°/176°)	2.98	0.1	4.29	0.0	3.15	0.1	4.41	0.0
E (175°/−2°)	2.05	0.6	2.32	0.4	2.20	0.5	2.41	0.3

[a] The glucose *gg* rotamers converge to conformer C′. [b] The glucose *gt* rotamers converge to conformer C.

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