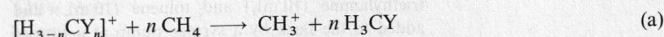


Tris(chalcogenato)carbenium Ions $[C(XR)_3]^+$ ($X = O, S, Se, Te$): An Experimental and Quantum-Chemical Comparison**

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Dedicated to Professor H. W. Roesky on the occasion of his 60th birthday

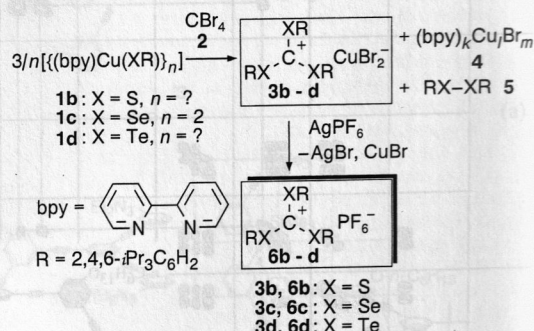
We have performed a systematic study of tris(chalcogenato)carbenium ions $[(RX)_3C]^+$ ($X = S, Se, Te$) to obtain a better understanding as to how donor atoms of the higher periods influence carbenium ion stability. Extensive experimental^[1] and theoretical^[2] studies have shown that carbenium ions $[H_{3-n}CY_n]^+$ can be stabilized by substituents Y ($Y = NR_2, PR_2, OR, SR, and halogen$) that contain electronegative heteroatoms with lone pairs that may engage in π donation as well as by substituents Y ($Y = Li, Na, BeH$) with electropositive elements which act as σ donors. In general, the stabilization energies (SE) can be quantified by the reaction energies of the hydride-transfer reactions [Eq. (a)] and the respective values for the cations $[H_{3-n}C(XH)_n]^+$ ($X = O, S, Se, Te; n = 1, 2, 3$) are listed in Table 1.



The oxocarbenium ion $[H_2C(OH)]^+$ ($SE \approx 64 \text{ kcal mol}^{-1}$; see also^[1d, 2e-g]) has almost the same stabilization energy as the $[H_2C(XH)]^+$ ions ($SE \approx 64-68 \text{ kcal mol}^{-1}$; see also^[1d, 2e-g]). The stabilization energies increase as the number of XH groups in the ions $[H_{3-n}C(XH)_n]^+$ increase. This increase is about the same for the thio-, seleno-, and telluro-

tuted ions (average values: $\Delta SE(1 \rightarrow 2) = 22.3 \text{ kcal mol}^{-1}$; $\Delta SE(1 \rightarrow 3) = 33.3 \text{ kcal mol}^{-1}$; where $\Delta SE(1 \rightarrow 2) = SE[HC(XH)_2]^+ - SE[H_2C(XH)]^+$ and $\Delta SE(1 \rightarrow 3) = SE[C(XH)_3]^+ - SE[H_2C(XH)]^+$). The SE values increase particularly for the ions $[HC(OH)_2]^+$ and $[C(OH)_3]^+$ ($\Delta SE(1 \rightarrow 2) = 40.7 \text{ kcal mol}^{-1}$ and $\Delta SE(1 \rightarrow 3) = 71.5 \text{ kcal mol}^{-1}$), and these ions are significantly more stabilized (by about 18 and 38 kcal mol^{-1} , respectively) than the homologous S, Se, and Te ions. These results are surprising in light of the decrease of the electronegativity $\chi_{\text{spec}}^{[3]}$ in the order $O \gg S > Se > Te$ and of the concomitant increases of the σ - as well as of the π -donating ability of the heteroatom X.^[2a, c] On the other hand, the χ_{spec} values of S, Se, and Te are relatively similar and we report herein experimental results that suggest that the bonding situations in the ions $[C(XR)_3]^+$ ($X = S, Se, Te$) also are comparable to each other, while they are clearly distinct from those in the $[C(OR)_3]^+$ ions.

Since the usual synthetic routes for the preparation of $[C(XR)_3]^+$ cations with $X = O, S$ by protonation or alkylation of $(RX)_2C=X$ cannot be extended to the selenium and tellurium compounds, we have devised a new synthesis for these cations (Scheme 1). The copper complexes **1b, c** can be prepared in situ



Scheme 1. Synthesis of **3b-3d** and **6b-6d**.

Table 1. Stabilization energies (SE) [a] at the QCISD(T,full)/LANL1DZ+P//MP2(full)/LANL1DZ+P' level.

Molecule [b]	Element X			
	O	S	Se	Te
$[C(XH)_3]^+$	135.31	100.37	96.55	100.79
$[HC(XH)_2]^+$	104.56	89.00	86.01	89.61
$[H_2CXH]^+ [c]$	63.83	65.65	64.40	67.72

[a] SE calculated as the reaction energy ΔE_{HTR} of the hydride transfer reaction: $[H_{3-n}C(XH)_n]^+ + nCH_4 \rightarrow [H_3C]^+ + nH_3C(XH)$. [b] Trisubstituted cations in C_{3h} symmetry; di- and monosubstituted cations in C_s symmetry. All energies in kcal mol^{-1} . [c] In good agreement with results obtained at comparable levels and reported in ref. [2g].

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by addition of 2,2'-bipyridine to the copper chalcogenolates $[Cu(XR)]$ ($X = S, [4] Se; [5] R = 2,4,6-iPr_3C_6H_2$) and **1d** can be obtained by reaction of $\{[(bpy)CuBr_2]\}_n$ ^[6] with $[(thf)_2LiTeR]$.^[7] The complexes **1b-d** react with CBr_4 (**2**) in CH_3CN (**1b, c**) or toluene (**1d**) to form the desired carbenium ions **3b-d** with dibromocuprate counterions. Exchange of the $CuBr_2^-$ ion by the PF_6^- ion yields the salts **6b-d** as yellow (**6b**), orange (**6c**), and pink (**6d**) solids, respectively. The corresponding oxocarbenium ion $[C(OR)_3]^+$ with $R = 2,4,6-iPr_3C_6H_2$ has not yet been prepared, but many such ions with other R groups were prepared by alkylation of carbonates and are well characterized. The salts **3b-d** and **6b-d** are remarkably soluble in apolar solvents such as benzene and Et_2O and can be handled in air.

The result of a single-crystal X-ray structure determination of **6d** is shown in Figure 1.^[8] Selected average distances and angles of **6d** are listed in Table 2 together with the respective data for the cations of **3b, c**.^[9] The central carbon atom in all of the cations of **3b, c** and **6d** is coordinated in a trigonal-planar fashion (sum of angles at the carbon center = 360°) and the X-C-X angles vary only marginally ($119.0^\circ-121.3^\circ$). The C-X-C angles decrease in the series $S > Se > Te$ as expected (**3b**: 102.5° ; **6c**: 97.8° , **6d**: 93.6°). Remarkably, the X-C bond to the central carbon atom C1 is shortened by about the same percentage (3.4-4.3%) in all cations. For the calculation of these percentages, we employed the X-C_{aryl} bonds as internal standard for the X-C(sp²) bond length. This indicates that the S-C, Se-C,

Table 2. Selected bond lengths [\AA] and angles [$^\circ$] for the cations of **3b,c**, **6d**, and **7a–d**. The Δ values specify the percentage shortening of the C1–X bond relative to the $C_{\text{aryl}}\text{--X}$ bond. The calculated values (in italics) for **7a–d** were obtained at the MP2(full)/LANL1DZ+P' level. The redox potentials for **6b–d** were measured in $\text{CH}_3\text{CN}/n\text{Bu}_4\text{NPF}_6$ with a Pt electrode using a Ag electrode with ferrocene as standard. A reversible redox wave ($\Delta E = 0.85$ mV) was observed in the cyclic voltammogram for **6b** at $T = 298$ K and for **6c,d** at $T = 238$ K.

Cmpd.	X	$d(\text{C1--X})$	$d(C_{\text{aryl}}\text{--X})$	$\angle (\text{C--X--C(H)})$	Δ [%]	$\delta(^{13}\text{C})$	$\delta(\text{X})$	$\lambda_{\text{max}}/\epsilon$ [nm]/ [eL mol $^{-1}$ cm $^{-1}$]	E_p^{red} [V]	E_{HOMO} [eV]	E_{LUMO} [eV]	ΔE [eV]
6a	O	—	—	—	—	166.3[b]	—	<190[c]	—	—	—	—
7a	O	1.289	—	102.5	5.9[a]	—	—	—	—	–21.99	–2.10	19.89
3b/6b	S	1.706	1.767	102.5	3.4	239.5	—	309/31 065	–0.68	–16.13	–4.72	11.41
7b	S	1.710	—	97.8	—	—	—	—	—	—	—	—
3c/6c	Se	1.839	1.933	97.8	4.9	253.7	^{77}Se : 770	388/16 835	–0.65	–14.77	–4.69	10.08
7c	Se	1.855	—	95.8	—	—	—	—	—	—	—	—
6d	Te	2.049	2.142	93.6	4.3	230.6	^{125}Te : 1279	500/22 940	–0.67	–13.15	–4.70	8.45
7d	Te	2.050	—	94.6	—	—	—	—	—	—	—	—

[a] The calculated percent shortening Δ is based on a $C_{\text{aryl}}\text{--O}$ distance of 1.370 \AA [10]. [b] Ref. [11 a]. [c] Refers to $[\text{C}(\text{OMe})_3][\text{BF}_4]$ [11 b].

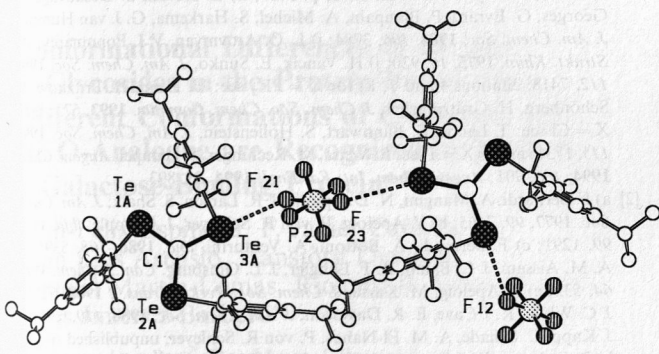


Fig. 1. SCHAKAL drawings of the two $[\text{C}(\text{TeR})_3][\text{PF}_6]$ complexes ($R = 2,4,6\text{-iPr}_3\text{C}_6\text{H}_2$) in the asymmetric unit of **6d** which are connected through one shorter (3.061 (15) \AA) and one longer Te–F (3.637 (15) \AA) contact. Selected averaged distances and angles are given in Table 2.

and Te–C bonds are electronically rather similar in these cations. This expectation can be corroborated by experimental results: a) The chemical shifts of the central carbon atom C1 (Table 2) fall in the same range for all cations; b) cyclic voltammetry in acetonitrile/ $n\text{Bu}_4\text{NPF}_6$ electrolytes showed nearly identical peak potentials at about -0.66 V for the reductions of the cations. These observations suggest that the LUMO energies—which depend on the (p-p) π interactions between the donor atom X and the acceptor atom C1—deviate from each other only marginally in all cations of **6b–d**. On the other hand, the lowest energy absorptions in the UV/Vis spectra of the salts **6b–d** exhibit a bathochromic shift of 79 nm when S is replaced by Se and a further shift of 112 nm when Se is replaced by Te (Table 2). Evidently, an increasing destabilization of the HOMO is associated with varying the X atom in the series S, Se, and Te. In contrast, the ^{13}C NMR signal of protonated carbonic acid $[\text{C}(\text{OH})_3]^+$ (**6a**) occurs at significantly higher field (Table 2), and no absorptions with wavelengths above 190 nm are observed in the UV/Vis spectra of tris(alkoxy)carbenium ions.^[11b] In these compounds the HOMO–LUMO gap thus is significantly larger.

The experimental observations are consistent with calculations of the cations $[\text{C}(\text{XH})_3]^+$ **7a–d** at the MP2(full)/LANL1DZ+P' level^[12] (Table 2) which establish strict C_{3h} symmetry for all of the trigonal-planar monocations and demonstrate excellent agreement between theoretical and experimental bond lengths and angles (average deviations are <0.01 \AA and $<3^\circ$, respectively). Information about the bonding situations and, for example, the size of the atoms in the molecules can be obtained from a topological electron density analysis (TEDA). TEDA is based on properties of the gradient vector field of the electron density distributions in Cartesian space and, in Figure 2, the gradient vector fields are exemplified for **7a** and **7b**.

The corresponding plots for the Se- and Te-containing cations greatly resemble the plot for **7b**. It becomes immediately apparent that the “bond critical points” (BCPs) for the C–X bonds (X = S, Se, Te) are closer to the X atoms than to the C atoms, which is in sharp contrast to the C–O bond in **7a**. The electron densities at the locations of the bond critical points (ρ_b) decrease in the series $\text{O} > \text{S} > \text{Se} > \text{Te}$. These TEDA results clearly demonstrate the umpolung of the C–X bond on going from the second to the third period and allow for an interpretation of the SE values (Table 1). As was previously described by Bernardi et al.,^[12c] the stabilization of the RO-substituted carbenium ions can largely be attributed to the high polarity of the $\text{C}^{\delta+}\text{--O}^{\delta-}$

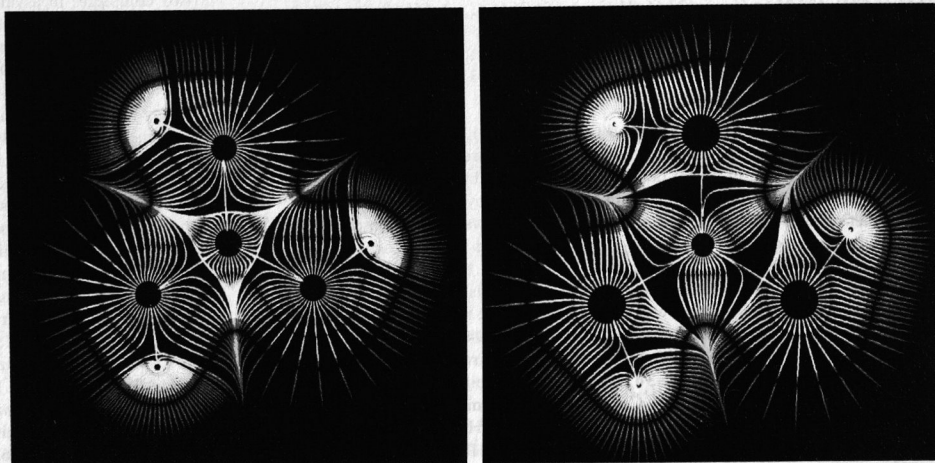


Fig. 2. Graphical representations of the gradient vector fields of the electron density distributions in the ions $[\text{C}(\text{OH})_3]^+$ (**7a**, left) and $[\text{C}(\text{SH})_3]^+$ (**7b**, right). The color coding reflects the magnitude of the electron density (pink 3–0.7, blue 0.35–0.3, yellow 0.2–0.1, red 0.05–0.01 $e a_0^{-3}$). The bond paths and the cross sections of the zero-flux surfaces also are shown and the bond critical points occur at their intersections.

bonding in the cations $[H_{3-n}C(OR)_n]^+$. This bond polarity results in spite of significant $X \rightarrow C$ π -bonding contributions, which, however, do not suffice to compensate the stronger $C \rightarrow X$ electron density shifts in the σ system. Consequently, instead of the expected charge dispersal an increased charge separation occurs. This interpretation also is consistent with the particularly large increase of the stabilities of the oxocarbenium ions ($X = O$) with increasing n in $[H_{3-n}C(XR)_n]^+$ ions because the Coloumb term contributes significantly to the binding energy in this case and increases the stability compared to the neutral compound $HC(XH)_3$. In contrast, the homologous cations $[R_{3-n}C(XR)_n]^+$ are stabilized by σ - and π -dative $X \rightarrow C$ bonding. Again an increasing electron density shift to the C atom is observed in the series $S < Se < Te$ which goes beyond formal charge dispersal and results in $X\delta^+ - C\delta^-$ bond polarizations that contribute to the stability of the cations. The nearly equal SE values of the $[H_2C(XH)]^+$ cations are fortuitous and result from different mechanisms of charge stabilization, which becomes clear only when the SE values associated with multiple substitution are considered.

Experimental Procedure

6b, c: $Cu(XR)$ (3.35 mmol) (1.00 g **1b** or 1.16 g **1c**) was dissolved in acetonitrile (50 mL) and treated with freshly sublimed 2,2'-bipyridine (3.35 mmol, 523 mg). The deep red solution was cooled to 0 °C and a solution of CBr_4 (372 mg, 1.12 mmol) in acetonitrile (5 mL) was added by syringe over the course of 1 min. The solution was stirred overnight at room temperature. The resulting precipitate was separated by using a filtering crucible (fritted glass disk D4), and the acetonitrile was removed under vacuum. The dark, oily residue was stirred with warm hexane (3×10 mL) and after this treatment the yellow crude product **3b, c** was obtained after drying under high vacuum. The crude product was treated with $AgPF_6 \cdot 2CH_3CN$ (for **3b** (211 mg, 0.63 mmol), for **3c** (270 mg, 0.81 mmol)) in THF (20 mL) in the dark. After the mixture had been stirred for 1 h, the THF was removed under high vacuum, the residue was taken up in CH_2Cl_2 (20 mL), and the solution was filtered through silica. CH_2Cl_2 was removed under high vacuum and the remaining solid was washed with hexane and dried. **6b:** Yield 542 mg (56%) (m.p. 211 °C); 1H NMR ($CDCl_3$): $\delta = 1.19$ (d, 18 H, $J(H,H) = 6.8$ Hz, $o-CH_3$), 1.27 (d, 18 H, $J(H,H) = 6.8$ Hz, $p-CH_3$), 1.42 (d, 18 H, $J(H,H) = 6.8$ Hz, $o-CH_3$), 3.03 (m, 9 H, $J(H,H) = 6.8$ Hz, o - and $p-CH$), 7.27 (s, 6 H_{ar}); ^{13}C NMR ($CDCl_3$): $\delta = 23.29$ and 23.57 ($o-CH_3$), 25.04 ($p-CH_3$), 32.97 ($o-CH$), 34.44 ($p-CH$), 117.22 ($p-C_{ar}$), 124.50 ($H-C_{ar}$), 152.73 ($o-C_{ar}$), 156.52 ($ipso-C_{ar}$), 239.51 ($C_{central}$); ^{31}P NMR ($CDCl_3$): $\delta = -144.5$ (m, $J(P,F) = 711$ Hz); ^{19}F NMR ($CDCl_3$): $\delta = -74.4$ (d, $J(F,P) = 711$ Hz); UV (Et_2O) $\lambda_{max}(\epsilon)$: 214 (60810), 256 (59310), 309 (31065), 375 nm (5665) strong offset shoulder. **6c:** Yield 809 mg (72%) (>185 °C decomp.); 1H NMR ($CDCl_3$): $\delta = 1.19$ (d, 18 H, $J(H,H) = 6.8$ Hz, $o-CH_3$), 1.28 (d, 18 H, $J(H,H) = 6.8$ Hz, $p-CH_3$), 1.39 (d, 18 H, $J(H,H) = 6.8$ Hz, $o-CH_3$), 2.98 (m, 3 H, $J(H,H) = 6.8$ Hz, $p-CH$), 2.99 (m, 6 H, $J(H,H) = 6.8$ Hz, $o-CH$), 7.29 (s, 6 H_{ar}); ^{13}C NMR ($CDCl_3$): $\delta = 22.73$ and 22.83 ($o-CH_3$), 24.01 ($p-CH_3$), 33.43 ($p-CH$), 34.16 ($o-CH$), 123.25 ($p-C_{ar}$), 123.66 ($H-C_{ar}$), 151.26 ($o-C_{ar}$), 155.03 ($ipso-C_{ar}$), 253.71 ($C_{central}$); ^{77}Se NMR ($CDCl_3$): $\delta = 769.5$; ^{31}P NMR ($CDCl_3$): $\delta = -144.4$ (m, $J(P,F) = 712$ Hz); ^{19}F NMR ($CDCl_3$): $\delta = -74.0$ (d, $J(F,P) = 712$ Hz); UV (Et_2O) $\lambda_{max}(\epsilon)$: 208 (63265), 254 (40490), 343 (9565) shoulder, 388 nm (16835).

6d: [(thf) $_3$ LiTeR] (1.61 g, 3.35 mmol) and [(bipy)CuBr] $_2$ (1.00 g, 1.67 mmol) were mixed and THF (50 mL) was added at -80 °C. The mixture was allowed to warm to -30 °C and stirred until a clear deep red solution was obtained. At 0 °C, half of the THF was removed under high vacuum and replaced by toluene. The solution was further reduced to about 15 mL and toluene (25 mL) was added subsequently. This solution was stored overnight at -70 °C. Precipitated LiBr was separated by filtration (fritted filter D4). The red-brown solution was brought to 0 °C and a solution of CBr_4 (372 mg, 1.12 mmol) in toluene (5 mL) was added by syringe over the course of 1 min. The solution was stirred overnight at room temperature, the resulting solid was separated by filtration (fritted filter D4) and toluene was removed in a high vacuum. The residue was stirred with warm hexane (3×10 mL). After drying in high vacuum, crude **3d** was obtained as a pink solid. As with **6b, c**, **6d** was prepared with $AgPF_6 \cdot 2CH_3CN$ (128 mg, 0.38 mmol). **6d:** Yield 437 mg (34%) (m.p. 152 °C); 1H NMR (C_6D_6): $\delta = 1.16$ (d, 18 H, $J(H,H) = 6.8$ Hz, $o-CH_3$), 1.26 (d, 18 H, $J(H,H) = 6.8$ Hz, $p-CH_3$), 1.39 (d, 18 H, $J(H,H) = 6.8$ Hz, $o-CH_3$), 2.89 (m, 3 H, $J(H,H) = 6.8$ Hz, $p-CH$), 3.11 (m, 6 H, $J(H,H) = 6.8$ Hz, $o-CH$), 7.37 (s, 6 H_{ar}); ^{13}C NMR (C_6D_6): $\delta = 23.92$ ($p-CH_3$), 24.92 and 25.05 ($o-CH_3$), 34.70 ($p-CH$), 40.08 ($o-CH$), 124.61 ($H-C_{ar}$), 129.83 ($p-C_{ar}$), 154.60 ($o-C_{ar}$), 155.58 ($ipso-C_{ar}$), 230.39 ($C_{central}$); ^{125}Te NMR (C_6D_6): $\delta = 1278.8$; ^{31}P NMR (C_6D_6): $\delta = -145.0$ (m, $J(P,F) = 714$ Hz);

^{19}F NMR (C_6D_6): $\delta = -75.0$ (d, $J(F,P) = 714$ Hz); UV (Et_2O) $\lambda_{max}(\epsilon)$: 210 (65415), 275 (34565), 361 (2705), 500 nm (22940).

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Conformational Differences of O- and C-Glycosides in the Protein-Bound State: Different Conformations of C-Lactose and Its O-Analogue are Recognized by Ricin B, a Galactose-Binding Protein**

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Dedicated to Prof. Dr. Manuel Bernabé on the occasion of his 60th birthday

The interest in the chemistry of C-disaccharides as structural analogues of O-glycosides continues to grow^[1] since these carbon-bridged compounds are thought to affect the activity of glycosidases as competitive inhibitors of the natural compounds. Therefore, it is extremely important that both compounds, the natural substrate and its C-glycoside analogue, are recognized by the enzyme in a similar way. The conformation of free C-glycosides has usually been assumed to be the same as that of the corresponding O-analogues.^[2] However, we have recently demonstrated that, at least for O- and C-lactoses, this is not the case.^[3]

To the best of our knowledge, it is not yet known whether both compounds are recognized by a carbohydrate-binding protein in the same conformation. Apart from the presence of the key interacting groups in the nonnatural substrate, this would be an essential requirement for an important inhibitory activity. On this basis, we report now on the use of 2D transferred NOE (TR-NOESY) and transferred ROE (TR-ROESY) experiments^[4] to study the complexation of C-lactose (**1**) by a galactose-binding protein, ricin B.^[5] In addition, we compare the obtained results with those reported for the complexation of regular lactose analogues.^[6] Taking advantage of the large size of lectins, TR-NOE (TR-ROE) experiments have recently been

used to determine the 3D structure of protein-bound carbohydrates^[7] by focusing on the easily detected NMR signals of the free ligand.

Figure 1 shows compound **1** and its O-analogue, methyl α -lactoside (**2**), along with their atomic numbering. The glycosidic dihedral angles are defined as Φ (H1'-C1'-O1'(C₂)-C4) and Ψ (C1'-O1'(C₂)-C4-H4). We have recently reported on the conformational study of **1** and **2** using NMR spectroscopy and only the basic features will be presented here.^[3, 8] Both compounds adopt the *exo*-anomeric conformation around the glycosidic bonds but the conformation around the aglyconic bonds are rather different. For **2**, about 90% of the population is located in the central low-energy region (minimum A, Φ/Ψ 54/18), while roughly 10% of population presents similar Φ values but has Ψ values around 180° (minimum B, Φ/Ψ 36/180). These two different dispositions around the aglyconic bond are referred to as *syn* and *anti*, respectively.^[9a] However, for **1** approximately 55% of the population adopts the *anti* conformation, while about 40% presents the *syn* orientation. The experimental data also indicate that minimum C (Φ/Ψ 180/0) is also populated (ca. 5%). Therefore, C-lactose exhibits much higher flexibility than its O-analogue. Table 1 summarizes the exclusive NOEs^[9b] that characterize each region for **1**.

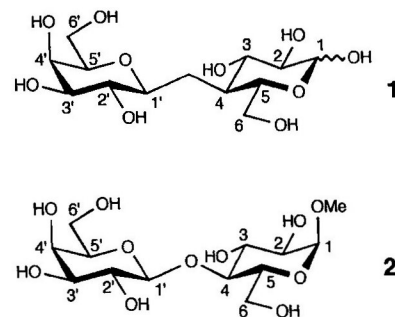


Fig. 1. Views of C-lactose (**1**) and methyl α -lactoside (**2**) showing the atomic numbering.

Table 1. Normalized NOESY and TR-NOESY intensities [%] for **1** at 30 °C in D₂O at (Varian, 500 MHz). The mixing times for the NOESY and TR-NOESY experiments were 700 and 300 ms, respectively.

Proton pair	NOE [%]	
	Free	Bound
H ^{pro-R} /H3	5.7	0.0
H ^{pro-S} /H5	3.0	0.0
H ^{pro-S} /H6 [a]	2.7	0.0
H1'/H4	2.1	-1.2
H1'/H3	5.9	-3.1
H ^{pro-R} /H6 [a]	5.1	-5.4

[a] These NOEs were obtained by adding the contributions of both H6 protons.

The conformational changes that occur when methyl α -lactoside is bound to ricin B have been studied using TR-NOESY and TR-ROESY experiments.^[6a] In summary, the bound conformation deviates slightly from the *exo*-anomeric conformation towards smaller Φ angles, while the orientation around the aglyconic bond is exclusively *syn*. The relevant interproton distances (H1'-H4 ca. 2.2.-2.3 Å) are in agreement with those reported previously for the binding of methyl β -lactoside to ricin.^[6b]

For C-lactose in the presence of ricin B the observed NOEs are negative, an indication of binding. The NOESY spectra of **1** (Fig. 2) recorded in the absence and in the presence of the lectin show important differences. First, the presence of both H1'/H3 and H^{pro-R}/H6 cross peaks, which define the population around minimum B, indicates that the *anti* conformation is indeed recognized by the protein, in contrast with the results

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