

Article

ANCHIMERIC ASSISTANCE IN EI-MS CARBOCATIONS – A COMPUTATIONAL INVESTIGATION*

Mihai-Cosmin Pascariu^{1,2}, Carmen-Manuela Mitar¹, Ioana-Ramona Ciopănoiu¹, Alexandra Gruia³, Mircea Niculescu^{2,4}, Eugen Sisu^{5*}

¹ “Vasile Goldiș” Western University of Arad, Faculty of Medicine, Pharmacy and Dental Medicine, Department of Pharmaceutical Sciences, 86 Liviu Rebreanu, 310045, Arad, Romania

² “Chemeia Semper” Association, 6 Giuseppe Verdi, 300493, Timișoara, Romania

³ Clinical County Hospital of Timișoara, Immunology of Transplant Department, 10 Iosif Bulbuca Blvd., 300736, Timișoara, Romania

⁴ University Politehnica Timișoara, Faculty of Industrial Chemistry and Environmental Engineering, 6 Vasile Pârvan Blvd., 300223, Timișoara, Romania

⁵ “Victor Babeș” University of Medicine and Pharmacy of Timișoara, Faculty of Medicine, Department of Biochemistry, 2 Eftimie Murgu Sq., 300041, Timișoara, Romania

ABSTRACT

A set of heptyl di-*O*-isopropylidene-D-mannofuranoside structures, which could find applications as biocompatible surfactant precursors in fields like pharmaceuticals and biotechnology, were analyzed using semi-empirical quantum chemical methods. Cations derived from them by removing one methyl group from the heptyl residue were constructed and conformationally optimized. Strong interactions between the sugar moiety oxygen atoms and the alkyl positively charged centers were detected in some cases, providing new cyclic enclosures which offer enhanced stability. The results obtained in this paper concern mainly the mass spectrometry analysis of side-chain glycoderivatives, but similarities can also be found for other oxygenated classes of compounds.

* Dedicated to Prof.Dr. Mihail Bîrzescu, in memoriam

* Correspondent author E-mail: sisueugen@umft.ro

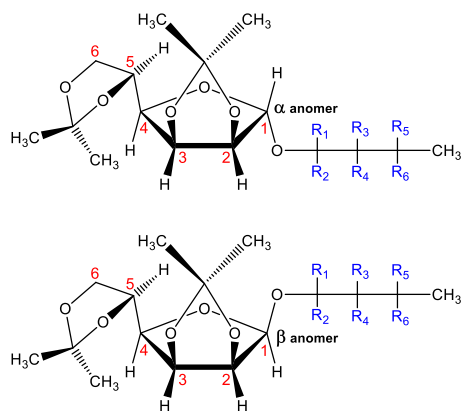
Keywords: glycoderivative, computational chemistry, RM1 semi-empirical method, heat of formation, carbocation, anchimeric assistance, dative bond, mass spectrometry.

1. INTRODUCTION

Sixty glycoderivatives possessing the 2,3:5,6-di-*O*-isopropylidene-D-mannofuranoside base structure, connected at the anomeric position to different alkyl side chains, were investigated using quantum chemical calculations [1,2]. These compounds, after simple hydrolysis of the isopropylidene acetal units [3], can function as biocompatible and biodegradable surfactants in many fields, particularly in pharmaceuticals, veterinary medicine and biotechnologies, but also as household nontoxic detergents [4].

The side chains include the following branched heptyl isomers: 1,1,2-trimethylbutyl (*R/S*), 1,1,3-trimethylbutyl, 1,2,2-trimethylbutyl (*R/S*), 1,2,3-trimethylbutyl (*R,R/R,S/S,R/S,S*), 2,2,3-trimethylbutyl, 1,3,3-trimethylbutyl (*R/S*), 2,3,3-trimethylbutyl (*R/S*), 1-ethyl-1-methylbutyl (*R/S*), 1-ethyl-2-methylbutyl (*R,R/R,S/S,R/S,S*), 1-ethyl-3-methylbutyl (*R/S*), 2-ethyl-1-methylbutyl (*R/S*), 2-ethyl-2-methylbutyl, 2-ethyl-3-methylbutyl (*R/S*), 1-propylbutyl and 1-isopropylbutyl (*R/S*). The general structures for the studied glycoderivatives are given in Figure 1. As can be seen, all the lateral chains are composed of a butyl main chain on which three other carbon atoms are linked as smaller chains (methyl, ethyl, propyl or isopropyl). The four carbon atoms linear core chain was specifically chosen to test for the possible formation of an anchimerically stabilized nine member ring, as explained further in this paper (in “Results and discussion” section). The study consists of removing one methyl radical from the side chain in all possible variants and calculating the heat of formation of the carbocation thus obtained with the help of the RM1 semi-empirical method [5].

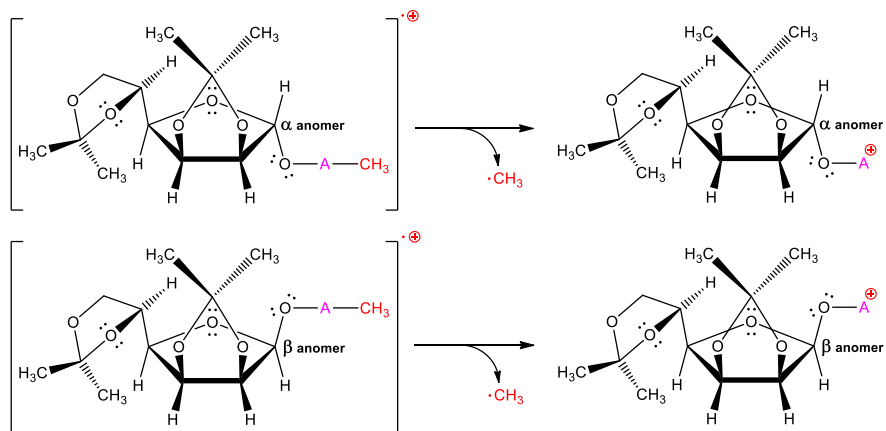
Figure 1: General structures of the studied mannofuranoside anomers; R₁-R₆ = H or short alkyl chains (methyl, ethyl, propyl or isopropyl)



Such carbocations [6-9] could be obtained in molecular fragmentation processes involved in the electron ionization mass spectrometric (EI-MS) analysis of this type of compounds, as seen in Figure 2 [4,10]. When some peaks found in the mass spectrum have an unexpected

high-intensity, one can propose the hypothesis of an anchimeric effect as a plausible explanation. Indeed, anchimeric-type stabilizations [11-14] spontaneously occurred after geometry optimization in some of the studied cations, with the formation of new three (oxirane), four (oxetane), five (1,3-dioxolane), six (1,3-dioxane) or nine (1,3,6-trioxonane) member cyclic structures [15-17]. This phenomenon could therefore have implications in peak patterns observed in EI-MS spectra of side chain glycoderivatives [4,18-21].

Figure 2: One possible way of producing $[M-15]^+$ cations from the radical cations in EI-MS fragmentation; A = alkylene group



2. METHODS

All structures were drawn using the *HyperChem* molecular modeling software [22] and were optimized with the RM1 semi-empirical method [5], with and without molecular mechanics pre-optimization. RHF operators were used for “Spin Pairing” while the SCF “Convergence limit” was set at 10^{-5} , without using the “Accelerate convergence” procedure. Force fields used for cations pre-optimization include MM+, AMBER99, BIO+ (CHARMM27) and OPLS, with their default parameters as implemented in *HyperChem*. For geometry optimization and ΔH_f calculation [14], the “Polak-Ribière (conjugate gradient)” algorithm was selected with a RMS gradient of 0.01 kcal/(Å mol), the molecules being considered in vacuum (*in vacuo*). The initial neutral molecules, from which all carbocations were constructed, were pre-optimized with the OPLS force field, followed by the RM1 semi-empirical method. All calculations were done with a system comprised of an *Intel® Core™2 Quad CPU Q8400@4x2.66 GHz* with 4 GB of RAM.

3. RESULTS AND DISCUSSIONS

For some of the studied carbenium ions, the positively charged carbon atom approached O1, O4 or O5 at a distance similar to a normal C-O single bond length ($\sim 1.47 \text{ \AA}$), while at the same time changing from sp^2 to sp^3 hybridisation and thus acting as a prochiral center (Figures 3 and 4). In Table 1 only the isomers that produced such an anchimeric-type stabilization are presented. The newly formed ring types are denoted as $3m$ (three member), $4m$ (four member), $5m$ (five member), $6m$ (six member) or $9m$ (nine member). All these interactions could be classified as *exo-tet*, according to Baldwin's rules [23-25].

Figure 3: Closing of 3-member (a, b) and 4-member (c, d) cycles; R_A - R_D = H or short alkyl chains

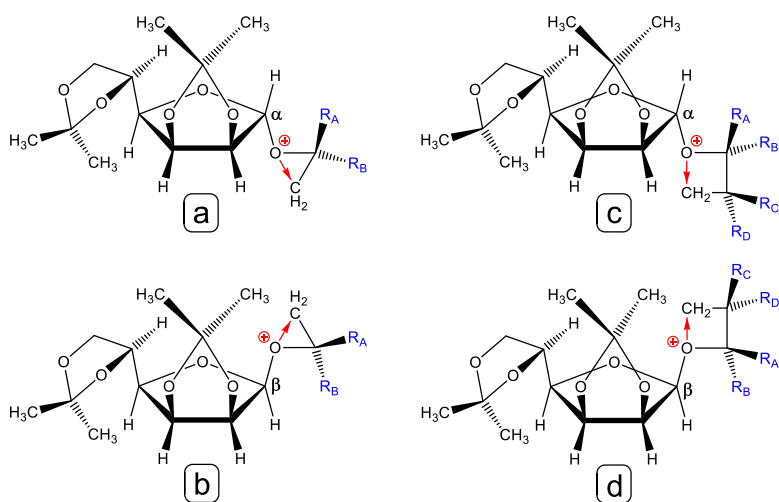


Figure 4: Closing of 5-member (a, b) and 6-member (c, d) cycles; R_A - R_D = H or short alkyl chains

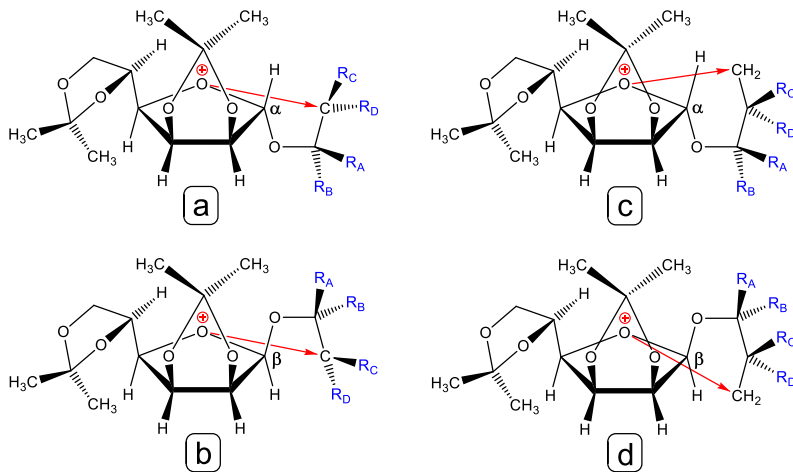


Table 1: Comparison between cation heats of formation and dative bond lengths; the type of ring formed (*3m*, *4m*, *5m*, *6m* or *9m*) is shown in parenthesis (see Figures 3 and 4), the values obtained for structures without anchimeric assistance (marked with “\$” sign) being also included for reference; oxygen atoms are numbered as for mannose, while the lateral chain carbon atoms and the hydrogen atoms attached to them are referenced in the table footnotes as α , β or γ , with increasing distance from O1

No.	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Conf.	RM1		RM1/MM+		RM1/AMBER99		RM1/BIO+		RM1/OPLS	
								C-O distance (Å)	$\Delta_f H$ (kcal/mol)	C-O distance (Å)	$\Delta_f H$ (kcal/mol)	C-O distance (Å)	$\Delta_f H$ (kcal/mol)	C-O distance (Å)	$\Delta_f H$ (kcal/mol)	C-O distance (Å)	$\Delta_f H$ (kcal/mol)
1	Me	H	Me	H	Me	H	α, S, R	1.477 (<i>5m</i>)	-117.606	1.479 (<i>5m</i>)	-117.430	F.O.	F.O.	1.479 (<i>5m</i>)	-117.430	1.477 (<i>5m</i>)	-115.993
2	Et	Me	H	H	H	H	α, R	1.462 (<i>5m</i>)	-117.606	1.462 (<i>5m</i>)	-117.961	1.463 (<i>5m</i>)	-117.757	1.462 (<i>5m</i>)	-117.757	1.462 (<i>5m</i>)	-117.757
3	Et	Me	H	H	H	H	β, R	1.401 (\$3m) ^a	-114.424	2.322 (\$3m) ^b	-133.381	1.400 (\$3m) ^a	-113.287	1.464 (<i>3m</i>)	-91.735	1.400 (\$3m) ^a	-113.287
4	Et	Me	H	H	H	H	α, S	1.399 (\$3m) ^a	-115.943	2.333 (\$3m) ^b	-133.502	1.401 (\$3m) ^a	-115.327	1.462 (<i>3m</i>)	-90.632	1.401 (\$3m) ^a	-115.327
5	Et	Me	H	H	H	H	β, S	1.463 (<i>5m</i>)	-112.889	1.460 (<i>5m</i>)	-110.796	1.463 (<i>5m</i>)	-112.889	1.463 (<i>5m</i>)	-112.889	1.463 (<i>5m</i>)	-112.889
6	Et	H	Me	H	H	H	α, R, R	4.142 (\$5m)	-98.024	1.481 (<i>5m</i>)	-114.275	3.814 (\$5m)	-97.922	4.174 (\$5m)	-98.727	1.481 (<i>5m</i>)	-114.276
								1.463 (<i>5m</i>)	-113.386	1.463 (<i>5m</i>)	-113.386	1.463 (<i>5m</i>)	-113.386	1.464 (<i>5m</i>)	-113.187	1.463 (<i>5m</i>)	-113.385
7	Et	H	Me	H	H	H	β, R, R	2.443 (\$3m) ^c	-135.216	2.436 (\$3m) ^c	-133.474	1.472 (<i>3m</i>)	-84.390	1.472 (<i>3m</i>)	-85.629	1.466 (<i>3m</i>)	-84.217
8	Et	H	Me	H	H	H	α, R, S	1.464 (<i>5m</i>)	-112.835	1.464 (<i>5m</i>)	-112.834	1.464 (<i>5m</i>)	-112.835	1.464 (<i>5m</i>)	-112.835	1.463 (<i>5m</i>)	-113.032
9	Et	H	Me	H	H	H	α, S, R	2.052 (\$5m)	-107.996	3.066 (\$5m)	-103.712	1.482 (<i>5m</i>)	-116.950	1.482 (<i>5m</i>)	-116.728	3.063 (\$5m)	-103.712
								1.471 (<i>3m</i>)	-84.529	2.343 (\$3m) ^d	-123.001	2.342 (\$3m) ^d	-123.998	2.344 (\$3m) ^d	-123.004	1.471 (<i>3m</i>)	-84.528
10	Et	H	Me	H	H	H	β, S, R	1.466 (<i>5m</i>)	-107.213	2.832 (\$5m)	-85.923	1.466 (<i>5m</i>)	-107.389	1.467 (<i>5m</i>)	-106.154	1.466 (<i>5m</i>)	-107.389
11	Et	H	Me	H	H	H	α, S, S	1.482 (<i>5m</i>)	-116.950	3.063 (\$5m)	-103.712	1.482 (<i>5m</i>)	-116.950	1.481 (<i>5m</i>)	-116.905	1.480 (<i>5m</i>)	-117.114
								2.342 (\$3m)	-81.550	1.471 (<i>3m</i>)	-85.217	1.470 (<i>3m</i>)	-85.333	1.471 (<i>3m</i>)	-85.065	1.473 (<i>3m</i>)	-85.136
12	Et	H	Me	H	H	H	β, S, S	1.465 (<i>5m</i>)	-108.554	1.465 (<i>5m</i>)	-108.555	1.465 (<i>5m</i>)	-108.555	1.465 (<i>5m</i>)	-108.554	1.465 (<i>5m</i>)	-108.554
13	Et	H	H	H	Me	H	α, R	2.807 (\$5m) ^e	-135.496	1.464 (<i>5m</i>)	-113.613	2.661 (\$5m)	-86.563	2.722 (\$5m)	-86.810	1.462 (<i>5m</i>)	-113.828
14	Et	H	H	H	Me	H	β, R	2.442 (\$3m) ^e	-135.758	1.471 (<i>3m</i>)	-86.633	2.442 (\$3m) ^e	-135.757	1.471 (<i>3m</i>)	-86.632	1.468 (<i>3m</i>)	-85.873
15	Et	H	H	H	Me	H	α, S	2.443 (\$3m) ^e	-135.990	1.470 (<i>3m</i>)	-85.779	2.340 (\$3m) ^e	-123.044	2.311 (\$3m)	-83.169	1.470 (<i>3m</i>)	-85.780
16	Et	H	H	H	Me	H	β, S	4.453 (\$5m) ^e	-133.606	1.465 (<i>5m</i>)	-109.084	4.100 (\$5m) ^e	-134.621	1.465 (<i>5m</i>)	-109.085	4.129 (\$5m) ^e	-135.126
17	Me	H	Et	H	H	H	α, R	2.730 (<i>4m</i>)	-87.945	1.481 (<i>4m</i>)	-105.813	1.481 (<i>4m</i>)	-105.813	1.481 (<i>4m</i>)	-105.814	1.481 (<i>4m</i>)	-105.814
18	Me	H	Et	H	H	H	β, S	1.488 (<i>4m</i>)	-106.979	1.488 (<i>4m</i>)	-106.979	4.554 (\$4m) ^f	-104.642	4.548 (\$4m) ^f	-104.875	1.488 (<i>4m</i>)	-106.980
19	H	H	Et	Me	H	H	β	2.706 (\$4m)	-86.418	1.491 (<i>4m</i>)	-106.207	2.676 (\$4m)	-86.416	2.679 (\$4m)	-86.416	2.675 (\$4m)	-86.416
20	H	H	Et	H	Me	H	α, R	1.478 (<i>6m</i>)	-114.539	3.303 (\$6m) ^g	-111.466	1.477 (<i>6m</i>)	-114.539	2.957 (\$6m) ^h	-115.985	1.476 (<i>6m</i>)	-114.861
21	H	H	Et	H	Me	H	β, R	1.464 (<i>6m</i>)	-107.275	1.464 (<i>6m</i>)	-109.808	3.932 (\$6m)	-89.095	F.O.	F.O.	3.934 (\$6m)	-89.095
22	H	H	Et	H	Me	H	α, S	1.464 (<i>6m</i>)	-114.738	1.464 (<i>6m</i>)	-114.738	1.464 (<i>6m</i>)	-114.739	1.464 (<i>6m</i>)	-114.738	1.464 (<i>6m</i>)	-114.739
23	H	H	Et	H	Me	H	β, S	2.739 (\$9m) ^h	-114.066	1.473 (<i>9m</i>)	-107.140	2.739 (\$9m) ^h	-114.229	2.741 (\$9m) ^h	-113.176	2.740 (\$9m) ^h	-114.230
24	Pr	H	H	H	H	H	α	3.755 (\$6m) ⁱ	-99.545	4.367 (\$6m) ^j	-101.126	1.459 (<i>6m</i>)	-114.989	3.900 (\$6m) ⁱ	-99.956	3.560 (\$6m) ^g	-107.886
25	Pr	H	H	H	H	H	β	1.460 (<i>6m</i>)	-110.261	2.891 (\$6m)	-97.068	1.487 (<i>4m</i>)	-102.843	1.460 (<i>6m</i>)	-110.261	1.487 (<i>4m</i>)	-102.842

No.	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Conf.	RMI		RMI/MM+		RMI/AMBER99		RMI/BIO+		RMI/OPLS	
								C-O distance (Å)	Δ _f H (kcal/mol)	C-O distance (Å)	Δ _f H (kcal/mol)	C-O distance (Å)	Δ _f H (kcal/mol)	C-O distance (Å)	Δ _f H (kcal/mol)	C-O distance (Å)	Δ _f H (kcal/mol)
26	i-Pr	H	H	H	H	H	α,R	3.750 (\$6m) ⁱ	-100.858	3.824 (\$6m) ^g	-108.940	4.865 (\$6m) ⁱ	-99.143	1.460 (6m)	-115.910	1.460 (6m)	-115.911
27	i-Pr	H	H	H	H	H	α,S	1.968 (\$5m) 1.483 (5m)	-106.482	1.486 (5m) 1.482 (5m)	-111.926 -117.407	3.641 (\$5m) 1.481 (5m)	-100.118 -117.300	1.971 (\$5m) 1.483 (5m)	-106.481 -117.208	2.810 (\$5m) 1.481 (5m)	-103.603 -117.301

F.O. = failed optimization;

^a rearrangement, see Figure 5;

^b rearrangement, see Figure 6 (C_α=O1 bond length: 1.291-1.295 Å) [26,27];

^c H_α→H_β, hydride shift, C_α=O1 double bond formed (1.285-1.297 Å) [26,27];

^d rearrangement, see Figure 7 (C_α=O1 bond length: 1.283-1.284 Å) [26,27];

^e rearrangement, see Figure 8 (C_α=O1 bond length: 1.284 Å) [26,27];

^f butene loss;

^g H_{β/β'} proton shift to O4 (furanose oxygen), C_{β/β'}=C_{γ'} double bond formed (1.328-1.331 Å);

^h H_β→H_γ, hydride shift;

ⁱ ethene loss;

^j H_γ→H_{γ'} hydride shift.

As observed from the heat of formation values, when compared with similar open-structure cations (marked with “\$” in Table 1), these enclosures imply increased stability (e.g., entries no. 10, 15, 17 and 21 in Table 1) [28].

Regarding the ring type abundance, the 1,3-dioxolane is the most abundant structure formed, being present in almost half of the stabilized structures, as can be seen in Table 2.

Figure 5: Rearrangement seen for entries 3 and 4 in Table 1

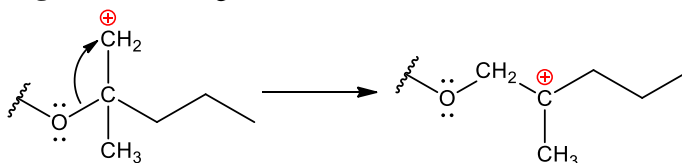


Figure 6: Rearrangement seen for entries 3 and 4 in Table 1

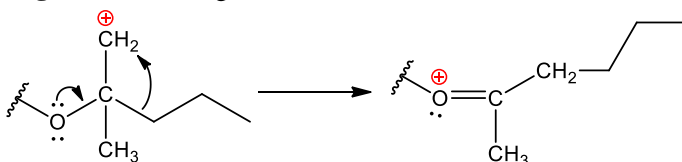


Figure 7: Rearrangement seen for entry 9 in Table 1

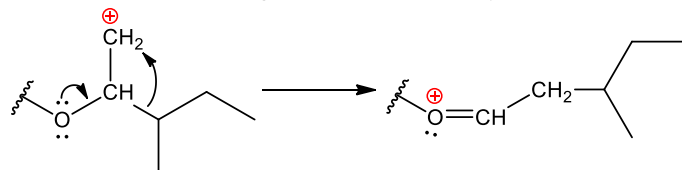
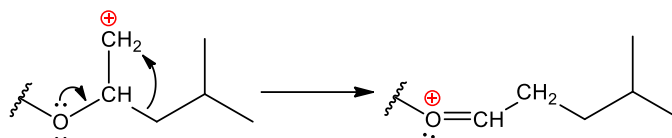


Figure 8: Rearrangement seen for entry 15 in Table 1**Table 2:** Ring statistics

Ring type/ ring closure	<i>3m</i> 3-exo-tet	<i>4m</i> 4-exo-tet	<i>5m</i> 5-exo-tet	<i>6m</i> 6-exo-tet	<i>9m</i> 9-exo-tet
Number of structures	7	4	12	6	1
C-O bond length (Å)	1.462 ÷ 1.473	1.481 ÷ 1.491	1.460 ÷ 1.486	1.459 ÷ 1.478	1.473
Dative C charge	-0.041 ÷ -0.015	0.022 ÷ 0.053	-0.056 ÷ 0.079	0.019 ÷ 0.055	0.047
Dative O charge	-0.177 ÷ -0.114	-0.173 ÷ -0.131	-0.162 ÷ -0.110	-0.190 ÷ -0.153	-0.167

Besides the heat of formation and the bond length values, another strong argument in favor of the anchimeric assistance is the charge distribution for the two atoms involved in the formation of the dative bond. A good example to illustrate this would be entry 25 in Table 1, corresponding to the 1-propylbutyl lateral chain in β configuration (see Figure 1, where R_1 =propyl, R_2 - R_6 =H). As can be seen in Table 1, two new stable rings can be formed, a *4m* (see Figure 3d, where R_A =propyl, R_B - R_D =H) and a *6m* ring (see Figure 4d, where R_A =propyl, R_B - R_D =H). While the calculated charge for the carbon atom is 0.444 for the open structure (marked with “\$” sign in Table 1), this drops to 0.055 when the *6m* ring is formed and to 0.053 when the *4m* ring is formed. Similarly, for the oxygen atom the charge corresponding to the open form is -0.290 (O1) / -0.336 (O4), and this rises to -0.186 (O4) for the *6m* ring and to -0.150 (O1) for the *4m* ring. Clearly a charge transfer has occurred, with the formation of the dative bond between the two atoms.

Table 3 shows the energy gain when the new rings are formed, by comparison with non-stabilized (open) structures. These values could also be interpreted as the dative bond energies: at least 2.6 kcal/mol for *3m* rings, 5.8 kcal/mol for *4m* rings, 9.0 kcal/mol for *5m* rings and 13.2 kcal/mol for *6m* rings. Also, the energy difference between a *4m* and a *6m* ring could be calculated, the *6m* ring being more stable by 7.4 kcal/mol. The obtained results generally agree with the literature concerning the stability of organic rings [15,29].

The majority of anchimerically stabilized structures are formed from primary carbocations (two hydrogens attached to the sp^2 positive carbon atom). Some secondary carbocations are also stabilized in this way but only giving five member rings, the resulting sp^3 geometry truly offering chiral properties to the dative carbon atom (entry 27 in Table 1, 5.481 kcal/mol difference between the two *5m* diastereomers formed). However, no tertiary carbocations took part in anchimeric stabilizations, probably because such species are already stabilized by the two extra alkyl radicals by donor inductive effects, and also because of the

steric crowding generated by the same radicals which could inhibit a favorable approach to the oxygen electron donor [30]. Also, a lot of decompositions were registered in the studied set of compounds, with various elimination products such as ethene, propene, butene or isobutene [31], and different proton and hydride shifts [32,33] were also frequently encountered. All this phenomena may have masked other cases of anchimeric stabilization.

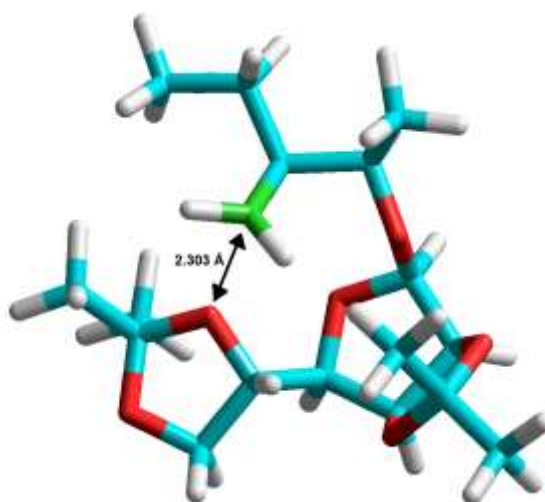
Table 3: Heat of formation differences, in kcal/mol (Table 1 entries from which these were calculated are given in parenthesis)

Open form* – 3 <i>m</i>	Open form* – 4 <i>m</i>	Open form* – 5 <i>m</i>	Open form* – 6 <i>m</i>	4 <i>m</i> – 6 <i>m</i>
3.783 (11)	17.869 (17)	15.549 (6)		
2.611 (15)	19.789 (19)	8.954 (9)	20.713 (21)	7.418 (25)
	5.775 (25)	21.466 (10)	13.193 (25)	
		13.402 (11)		
		27.018 (13)		
		10.925 (27)		

* structure in which, after geometry optimization, no anchimeric assistance was observed

Although we have found multiple computational evidence for anchimerically stabilized seven, eight or ten member rings in other related mannofuranose derivatives we have studied [34], only one nine member (1,3,6-trioxonane) cycle was produced to this day using this method (entry 23 in Table 1). However, we have also obtained the conformation shown in Figure 9 with one of the compounds considered in this paper ((*R*)-2-ethyl-1-methylbutyl initial lateral chain, β anomer), in which the sp^2 positive charged carbon atom approached O5 to a distance of 2.303 Å with a favorable atom arrangement but without becoming tetrahedral, suggesting the first step in a nine member ring closure.

Figure 9: Precursor to a nine member ring (formally charged carbon atom has sp^2 geometry)



4. CONCLUSIONS

Anchimerically stabilized rings with three to six members, along with a single nine-membered cyclic structure, were obtained *in silico* for different alkyl substituted glycoderivatives. The dative interaction between the formally positive carbon atom in the side chain and the oxygen atom from the mannose residue is revealed by the distance between the two atoms, similar to a normal C-O single bond, from heat of formation values, but also from the final charge repartition calculated using the RM1 semi-empirical method.

ACKNOWLEDGEMENTS

The authors would like to thank prof.dr. Mircea Mracec and prof.dr.eng. Nicolae Dincă for access to HyperChem software and also for fruitful discussions. This work was supported by the Romanian National Authority for Scientific Research (CNCS-UEFISCDI) through project PN-II-PCCA-2011-142.

REFERENCES

1. Box V.G.S., Evans-Lora T., “Exploring the relative reactivities of the hydroxyl groups of monosaccharides by molecular modeling and molecular mechanics”, *J. Mol. Struct.*, 516(2-3) (2000) 203-214.
2. Gerbst A.G., Grachev A.A., Shashkov A.S., Nifantiev N.E., “Computation techniques in the conformational analysis of carbohydrates”, *Russ. J. Bioorg. Chem.*, 33(1) (2007) 24-37.
3. Kohnstam G., Williams D.L.H., “Directive and activating effects of alkoxy and aryloxy groups in aromatic and aliphatic reactions” in (Patai S., Ed.) “The chemistry of the ether linkage, *PATAI'S Chemistry of Functional Groups*”, Ch. 3, John Wiley & Sons Ltd., London, 1967, p. 81-166.
4. Rafailă M., Pascariu M.C., Gruia A., Penescu M., Purcarea V.L., Medeleanu M., Rusnac L.M., Davidescu C.M., (2013) “GC-MS analysis of long chain mannofuranose derivatives as biocompatible surfactant precursors. Correlation between peak intensities and stability of corresponding fragments”, *Farmacia (Bucharest)*, 61(1) (2013) 116-126.
5. Rocha G.B., Freire R.O., Simas A.M., Stewart J.J.P., “RM1: A reparameterization of AM1 for H, C, N, O, P, S, F, Cl, Br, and I”, *J. Comput. Chem.*, 27(10) (2006) 1101-1111.
6. Olah G.A., “100 years of carbocations and their significance in chemistry”, *J. Org. Chem.*, 66(18) (2001) 5943-5957.

7. Carey F.A., Sundberg R.J., "Advanced organic chemistry. Part A: Structure and mechanisms", 5th edn., Springer Science+Business Media, LLC, New York, 2007.
8. Aue D.H., "Carbocations", *WIREs Comput. Mol. Sci.*, 1(4) (2011) 487-508.
9. Abboud J.L.M., Alkorta I., Dávalos J.Z., Müller P., Quintanilla E., "Thermodynamic stabilities of carbocations" in (Richard J.P., Tidwell T.T., Eds.) "Adv. Phys. Org. Chem.", Volume 37, Elsevier Science Ltd, London, 2002, p. 57-135.
10. Pascariu M.C., Sisu E., Ordodi V.L., Rusnac L.M., (2011) "Spectral analysis of diisopropylidenedated monosaccharides. Low energy EI-MS fragmentation study", *Chem. Bull. "Politehnica" Univ. (Timișoara)*, 56(1) (2011) 6-11.
11. Fărcașiu D., Leu R., "Theoretical studies of carbocations in ion pairs. 8. Search for anchimeric assistance in the ionization of 2-buthyl cation precursors", *J. Phys. Chem. A*, 112(13) (2008) 2955-2961.
12. Pale P., Vogel P., "Tricoordinate carbanions, cations and radicals" in (Katritzky A.R., Taylor R.J.K., Eds.) "Comprehensive organic functional group transformations II, Volume 1: Synthesis: Carbon with no attached heteroatoms", Ch. 1.19, Elsevier Ltd, 2004, p. 889-1017.
13. Ari J.B., Navon I., Mandelbaum A., "The effect of steric hindrance on the relative rates of anchimerically assisted alcohol eliminations from MH⁺ ions of 2-substituted 1,4-dialkoxybutanes upon CI and CID: Experiment and theory", *Int. J. Mass Spectrom.*, 249-250 (2006) 433-445.
14. Kimatrai M., Cruz-López O., García-Rubiño M.E., Morales F., Gómez-Pérez V., Campos J.M., "Neighboring-group participation involving the oxygen atom of the O,O- or O,N-acetal functional groups", *Curr. Org. Chem.*, 14(14) (2010) 1461-1477.
15. Eliel E.L., Wilen S.H., Mander L.N., "Stereochemistry of organic compounds", John Wiley & Sons, Inc., New York, 1994.
16. Bobylev V.A., Koldobskii S.G., Tereshchenko G.F., Gidasov B.V., "Nucleophilic reactions involving opening and closing of saturated heterorings (review)", *Chem. Heterocyc. Compd.*, 24(9) (1989) 947-959.
17. Kiprof P., Miller S.R., Achord P., "Dative stabilization of carbocations", *J. Mol. Struc.-Theochem*, 896(1-3) (2009) 69-72.
18. Mandelbaum A., "Stereochemistry studied using mass spectrometry" in (Lindon J.C., Tranter G.E., Holmes J.L., Eds.) "Encyclopedia of spectroscopy and spectrometry", Volume 1, Elsevier Ltd, 2000, p. 2211-2223.
19. Mutenda K.E., Matthiesen R., "Analysis of carbohydrates by mass spectrometry" in (Matthiesen R., Ed.) "Mass Spectrometry Data Analysis in Proteomics, Methods in Molecular Biology", Volume 367, Humana Press, 2007, p. 289-301.
20. De Jongh D.C., Biemann K., "Mass spectra of O-isopropylidene derivatives of pentoses and hexoses", *J. Am. Chem. Soc.*, 86(1) (1964) 67-74.
21. Morgenlie S., "Analysis of mixtures of the common aldoses by gas chromatography – mass spectrometry of their O-isopropylidene derivatives". *Carbohydr. Res.*, 41(1) (1975) 285-289.
22. HyperChem™ Professional, Hypercube, Inc., 1115 NW 4th Street, Gainesville, Florida 32601, USA
23. Alabugin I.V., Gilmore K., "Finding the right path: Baldwin "Rules for Ring Closure" and stereoelectronic control of cyclization", *Chem. Commun.*, 49(96) (2013) 11246-11250.

24. Gilmore K., Alabugin I.V., “Cyclizations of alkynes: revisiting Baldwin’s rules for ring closure”, *Chem. Rev.*, 111(11) (2011) 6513-6556.
25. Baldwin J.E., (1976) “Rules for ring closure”, *J. Chem. Soc. Chem. Comm.*, 1976(18) (1976) 734-736.
26. Miller S.R., Krasutsky S., Kiprof P., “Stability of carboxonium ions”. *J. Mol. Struct.-Theochem*, 674(1-3) (2004) 43-47.
27. Apeloig Y., Karni M., “The stabilities of α -oxy and α -thio carbenium ions: the importance of the ground-state energies of the neutral precursors”, *J. Chem. Soc. Perk. T. 2*, 1988(5) (1988) 625-636.
28. Benassi R., Taddei F., “Cyclic and open-chain carbonium ion intermediates in nucleophilic halogen displacement: 2-chloroethanol, 2-chloroethanethiol and their 1,3-propane homologues. A theoretical ab-initio MO approach”, *J. Mol. Struct.-Theochem*, 205 (1990) 177-190.
29. Mills J.A., “The stereochemistry of cyclic derivatives of carbohydrates” in (Wolfson M.L., Ed.) “Advances in carbohydrate chemistry”, Volume 10, Elsevier Inc., 1955, p. 1-53.
30. Capon B., McManus S.P., “Neighboring group participation”, Volume 1 withdrawn, Plenum Press, 1976, New York.
31. Bowen R.D., Williams D.H., “The concept of a hierarchy of unimolecular reactions in a homologous series. Prediction of the unimolecular chemistry of some saturated carbenium ions”, *J. Chem. Soc. Perk. T. 2*, 1976(13) (1976) 1479-1485.
32. Ahlberg P., Jonsäll G., Engdahl C., “Degenerate carbocation rearrangements” in (Gold V., Bethell D., Eds.) “Adv. Phys. Org. Chem.”, Volume 19, Academic Press Inc. Ltd, London, 1983, p. 223-379.
33. Planelles J., Sánchez-Marín J., Tomás F., Corma A., “A molecular orbital approach to a comprehensive cracking mechanism for linear long chain alkanes in heterogeneous acid catalytic conditions through carbenium ion β -cleavage”, *J. Chem. Soc. Perk. T. 2*, 1985(3) (1985) 333-340.
34. Pascariu M.C., Rafailă M., Medeleanu M., Badea V., Gruia A.T., Penescu M., Sisu E., “Computational search for long bonds in radical cations of sugars. 1. Glucofuranose, galactofuranose and mannofuranose di-*O*-isopropylidene derivatives”, *Farmacia* (2015), in press.