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QUANTUM CHEMISTRY OF CARBOHYDRATES

PART III. CALCULATION OF THE ELECTRONIC DISTRIBUTION IN SOME CARBOHYDRATE MOLECULES BY THE CNDO/2 METHOD

YU. A. ZHDANOV, V. I. MINKIN, R. M. MINJAEV, I. I. ZACHAROV, AND YU. E. ALEXEEV
Department of Chemistry, Rostov State University, Rostov-on-Don (U. S. S. R.)
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ABSTRACT

Calculations of the electronic distribution in α- and β-D-glucopyranose, β-D-arabinopyranose, and 2-deoxy-β-D-*erythro*-pentopyranose, as well as in the enediol form of D-*erythro*-pentulose and its dianion, have been performed by the CNDO/2 method, taking into account the exact geometry of the molecules. The results obtained are discussed in relation to the anomeric effect, dipole moment, ionization constants, and reactivity of the various sugars. The dipole moment of methyl α-D-glucopyranoside was also determined.

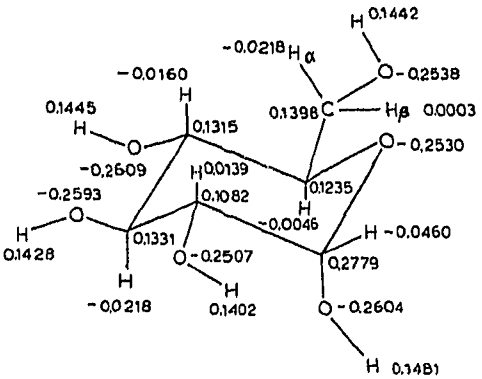
INTRODUCTION

Quantum mechanical calculations of the electronic distribution in cyclic and acyclic forms of pentoses[1,2] and other carbohydrates[3–5] have shown the utility of this approach for qualitative interpretation of chemical reactivity. These calculations involved the simplest methods of quantum chemistry, namely Hückel's method and Del Re's method of inductive parameters[6]. These methods consider only the bond sequence and do not take into account the geometry of the molecule. The resulting information is, therefore, of limited value, in that the electronic distributions in geometrical isomers are not distinguished and are critically dependent on the correct choice of empirical parameters.

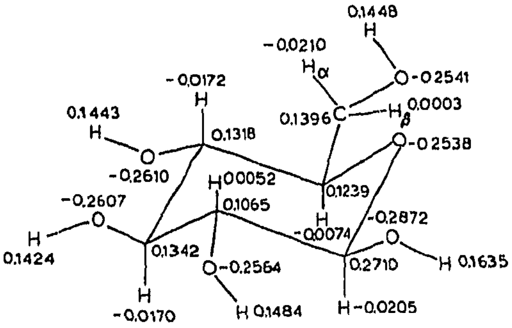
The present study describes the use of the SCFMO method, with neglect of differential overlap (CNDO/2[7] with the original parameters[8]), for calculation of the electronic structures and conformational energies of α- and β-D-glucopyranose, β-D-arabinopyranose, and 2-deoxy-β-D-*erythro*-pentopyranose (2-deoxy-D-ribose) as well as the enediol form of D-*erythro*-pentulose and its dianion. The SCFMO method is one of the most exact methods of quantum mechanical calculation for complex molecules, and is especially suitable for the calculation of electronic distribution in molecules containing atoms of the second period[8].

RESULTS AND DISCUSSION

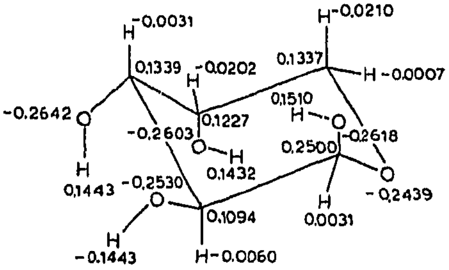
Since the application of the CNDO/2 method requires a knowledge of the exact molecular geometry, X-ray analysis data of some carbohydrates[9] have been used;



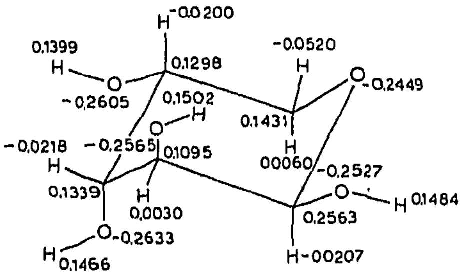
1 α-D-Glucopyranose *(C 1)*



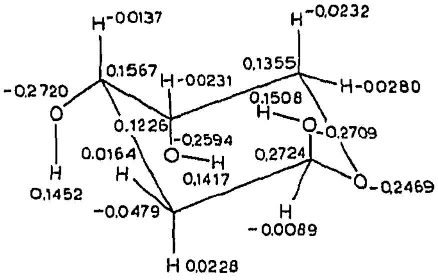
2 β-D-Glucopyranose *(C1)*



3 β-D-Arabinopyranose *(1C)*



4 β-D-Arabinopyranose*(C 1)*



5 2-Deoxy-β-D-*erythro*-pentopyranose *(1 C)*

the undetermined O–H and C–H bond lengths were taken to be 0.96 and 1.10 Å, respectively, and the most stable, *i.e. gauche*, conformation of vicinal hydroxyl groups was chosen in all cases. The number of molecules amenable to calculation is therefore limited, but the results obtained permit the recognition of certain correlations between the electronic structure and properties of carbohydrates.

The results of CNDO/2 calculations on some pento- and hexopyranoses are represented in formulae **1**–**5**. These results are in general agreement with those obtained previously[1–3], although some discrepancies of a quantitative character are observed (Tables I and II); the most noticeable of these involve the magnitude and sign of the charge on hydrogen atoms in C–H groups both in β-D-arabinopyranose (Table I) and α-D-glucopyranose (Table II). The absolute values of charges on oxygen and hydrogen atoms in hydroxyl groups are considerably smaller according to the CNDO/2 method in comparison with the values obtained by the Del Re method. Also, the former method gives the greater values of positive charge on C-1. Although the differences in charge values on the ring carbon atoms calculated by each method are minimal, certain trends are noticeable. The Del Re method indicates a decrease in the magnitude of positive charge from C-1 to C-5 (C-6), whereas, according to the CNDO/2 method, these charges alternate in magnitude.

Each method indicates that the maximum positive charge is present on C-1, and this situation may also be predicted qualitatively on the basis of the −I effects of O-1 and the ring oxygen atom. The greater value of the positive charge on C-1 in α-D-glucopyranose (**1**) than in the β-D anomer (**2**) is noticeable and is consistent with the axial hydroxyl group's having the greater −I effect.

Both methods indicated that the negative charge on O-1 is greater than that on the ring oxygen atom, thereby accounting for preponderant proton attack at the former site during the acid hydrolysis of glycosides[10]. Moreover, the greater negative charge on the equatorial O-1 in **2**, in comparison with that of the axial O-1 in **1**, affords a simple explanation of the well-known higher reactivity of β-D-glycosides towards acid hydrolysis[10], although the reverse anomeric effect[11] may be of some importance. The distribution of atomic charges in α- (**1**) and β-D-glucopyranose (**2**) also partially explains the exclusive interaction of β-D anomers with bromine[12] to give the respective aldonolactones.

Recently, the results of Del Re calculations on monosaccharides[1] were used[13] to explain mutarotation based on the concept of bifunctional catalysis. This explanation is also supported by the CNDO/2 calculations, since the hydrogen atom of HO-1 and the ring oxygen atom may be the centres of nucleophilic and electrophilic attack, respectively.

The decreased electronic density on H-2, as compared with those of the other hydrogen atoms in C–H groups [with the exception of H-1 of β-D-arabinopyranose (**3**) in the *1C* conformation], is possibly responsible for the known formation of oxyglycals from acetylated glycosyl halides by the action of amines.

The CNDO/2 calculations allow a correlation of the values of the positive charges (0.1481, 0.1635) on the hydrogen atoms of the anomeric hydroxyl groups in

TABLE I

COMPARISON OF ATOMIC CHARGES IN β-D-ARABINOPYRANOSE CALCULATED BY THE DEL RE[a] AND CNDO/2[b] METHODS

C-1	*C-2*	*C-3*	*C-4*	*C-5*	
0.1929	0.1162	0.1079	0.1069	0.0362	
0.2500	0.1094	0.1339	0.1227	0.1337	
C–H-1	*C–H-2*	*C–H-3*	*C–H-4*	*C–H-5*(α)	*C–H-6*(β)
0.0611	0.0525	0.0520	0.0518	0.0518	0.0518
0.0031	−0.006	−0.0031	−0.0202	−0.0007	−0.0210
O-1	*O-2*	*O-3*	*O-4*	*Ring oxygen*	
−0.4629	−0.4734	−0.4746	−0.4747	−0.2631	
−0.2618	−0.2530	−0.2642	−0.2603	−0.2439	
O–H-1	*O–H-2*	*O–H-3*	*O–H-4*		
0.3180	0.3164	0.3161	0.3161		
0.1510	0.1433	0.1443	0.1432		

[a] Upper lines of figures. The results have been obtained[1,2] in general for pyranoid pentose. [b] Lower lines of figures.

TABLE II

COMPARISON OF ATOMIC CHARGES IN α-D-GLUCOPYRANOSE CALCULATED BY THE DEL RE[a] AND CNDO/2[b] METHODS

C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	
0.1903	0.1143	0.1060	0.1040	0.0949	0.0450	
0.2779	0.1082	0.1334	0.1315	0.1235	0.1398	
C–H-1	*C–H-2*	*C–H-3*	*C–H-4*	*C–H-5*	*C–H-6*(α)	*C–H-6*(β)
0.0610	0.0528	0.0518	0.0516	0.0506	0.0530	0.0530
−0.0460	0.0139	−0.0218	−0.0160	−0.0046	−0.0218	0.0003
O-1	*O-2*	*O-3*	*O-4*	*O-6*	*Ring oxygen*	
−0.4462	−0.4568	−0.4580	−0.4583	−0.4566	−0.2619	
−0.2604	−0.2507	−0.2593	−0.2609	−0.2538	−0.2530	
O–H-1	*O–H-2*	*O–H-3*	*O–H-4*	*O–H-6*		
0.3034	0.3016	0.3014	0.3014	0.3017		
0.1481	0.1402	0.1428	0.1445	0.1442		

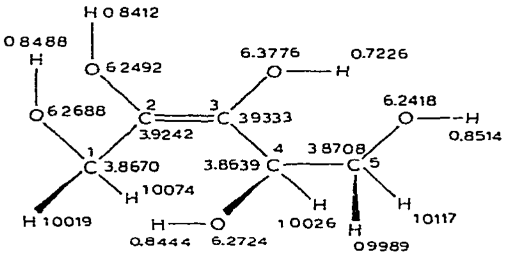
[a] Upper lines of figures. The results have been obtained[3] in general for pyranoid hexose. [b] Lower lines of figures.

α- and β-D-glucopyranose with the ionization constants (12.46, 12.17) of the respective anomers[14], suggesting that only glycosidic hydroxyl groups undergo ionization. Indeed, in alkaline solutions, D-glucopyranose exists almost wholly in the β form[15], which is, therefore, a much stronger acid than the α anomer.

Based on the data calculated herein, the dipole moments of α- and β-D-glucopyranose were found to be 3.9 and 3.5 D, respectively. These values differ significantly from the reported[16] experimental value of 14.1 D for D-glucose. In view of this discrepancy, the dipole moment of methyl α-D-glucopyranoside was determined and found to be 1.8 D which is in qualitative agreement with the calculated data.

The values of total energies afforded by the CNDO/2 calculations give an energy difference of 3.1 kcal.mole^{-1} for α- and β-D-glucopyranose. The experimental value[17] based on the anomeric equilibrium of D-glucopyranose in water is only 0.35 kcal.mole^{-1}. The divergence in the experimental and calculated values is possibly caused by solvation effects, as well as by uncertainties in location of the hydroxyl hydrogen atoms for the purpose of calculation. The calculated value (2.75 kcal.mole^{-1}) of the anomeric effect for D-glucopyranose differs considerably from the value of 0.55 kcal.mole^{-1} determined[17] by a semi-empirical method.

The increased negative charge on the carbon atom (C-2) of the deoxy group in **5** is of interest, since this phenomenon is undoubtedly responsible for the rapid glycosylation and deglycosylation of 2-deoxy sugars and their glycosides in acid medium owing to the stabilization of the intermediate glycosyl carbonium ion by the +*I* effect of the deoxy group.



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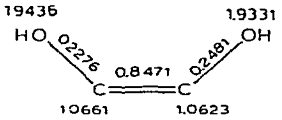
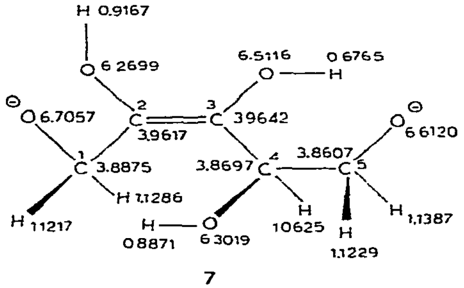


6a



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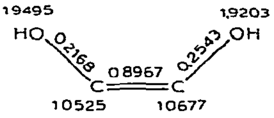
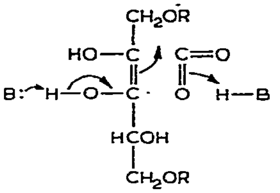


7a

The electronic distribution in the enediol form **6** of D-*erythro*-pentulose (D-ribulose) and in the dianion **7** has also been calculated, in an attempt to provide a better understanding of carbon dioxide fixation by ribulose 1,5-diphosphate during photosynthesis. The most probable conformations **6** and **7** were chosen for calculation, and the electronic charges are shown in the formulae. Such values are usually employed for charged species in contradistinction to uncharged molecules. The molecular diagrams **6a** and **7a** show the distribution of π-electronic density in **6** and **7**, respectively.

As seen from formulae **6** and **7**, the formation of the enediol grouping results in a decrease of the fractional positive charges on C-2 and C-3 in comparison with the other carbon atoms, and an increase of negative charge on O-3 with a simultaneous increase of positive charge on the adjacent hydrogen atom which, therefore, possesses an increased activity. These effects are intensified in the anion **7**.



$R = PO_3H_2$ or PO_3^{2-}

8

Hence, the nature of the proposed[18,19] transition state **8** as an initial step of carbon dioxide fixation becomes clearer since the attack of base is most probable on the proton of HO-3. This probability should be increased if ribulose 1,5-diphosphate reacts as the anion.

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