

THE APPLICATION OF MOLECULAR ORBITAL  
CALCULATIONS TO WOOD CHEMISTRY.  
II. THE PROTONATION OF  
BETA-METHYL GLUCOPYRANOSIDE<sup>1</sup>

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ABSTRACT

The protonation step in the acid hydrolysis reaction of beta-methyl glucopyranoside was studied by molecular orbital techniques. The semi-empirical, self-consistent fields method of modified neglect of diatomic overlap (MNDO) was used to calculate energetic and electronic information in an attempt to determine the site of initial protonation.

*Keywords:* Beta-methyl glucopyranoside, molecular orbital calculations, protonation.

INTRODUCTION

The previous paper in this series (Elder and Worley 1985) proposed the use of quantum chemical-molecular orbital calculations on the chemical constituents of wood. These types of studies are of interest for two reasons. First, this area represents a largely unexplored field of wood chemistry, which opens up a host of studies that may be performed. Second, it addresses molecular properties, an understanding of which could contribute to our knowledge of the macroscopic and material properties of wood.

Since cellulose is one of the most abundant organic chemicals on earth, it follows logically that the O-glucosidic bond is one of the most common chemical bonds. This bond is important structurally to carbohydrates in general and to cellulose in particular. Furthermore, the utilization of cellulose often requires cleavage of this bond, such that the glucose groups, of which the cellulose is composed, may be used for subsequent transformations. The cleavage reaction that comes most immediately to mind is the hydrolysis of cellulose, the reactants of which may then be subjected to fermentation for the production of fuels and chemicals. The hydrolysis reaction of glycosides has been extensively studied and has been reviewed by Bochkov and Zaikov (1979), Capon (1969), and BeMiller (1967). The initial problem to be considered concerns the route of the protonation. The proton may attack either the oxygen within the ring or the glycosidic oxygen, resulting

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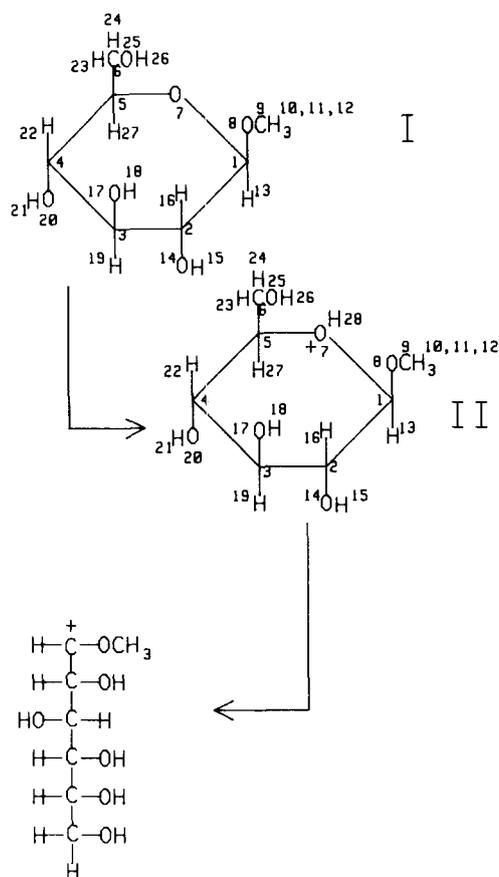


FIG. 1. Protonation of the ring oxygen to form an acyclic carbonium ion (after BeMiller 1967).

in an acyclic or cyclic carbonium ion, respectively (Figs. 1 and 2). The evidence that has been reported is still not completely conclusive, but it indicates that the probable mechanism involves the protonation of the glycosidic oxygen and formation of a cyclic carbonium ion. According to BeMiller (1967), the evidence for this route is not unquestionable, but there is little evidence favoring the alternate mechanism.

The object of the current report is to study this initial protonation by molecular orbital techniques in an attempt to elucidate the energetically or electronically preferred route. The anomeric position in carbohydrates has been the subject of a number of *ab initio* quantum mechanical studies (Jeffrey et al. 1972, 1974, 1978; Newton et al. 1979; Jeffrey and Yates 1979, 1980). These have largely been conformational studies, and of necessity examined model compounds rather than the carbohydrate itself.

#### METHODS

The computational procedure used in this paper is the semi-empirical, self-consistent fields (SCF) method of modified neglect of diatomic overlap (MNDO)

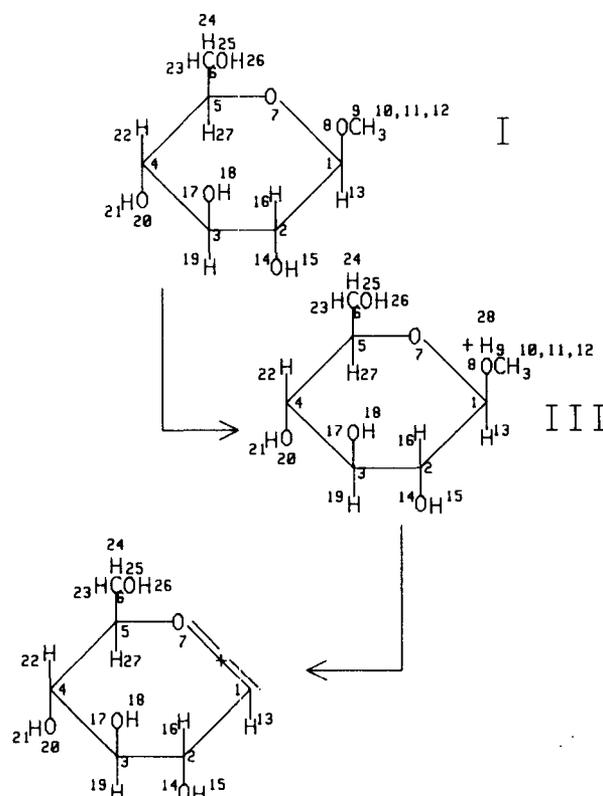


FIG. 2. Protonation of the glycosidic oxygen to form acyclic carbonium ion (after BeMiller 1967).

(Dewar and Thiel 1977a, b). There are a number of other computational methods available for these kinds of studies, but MNDO is the best available at the present time for large molecules. The method makes comparatively few assumptions and approximations, and calculates the optimum geometry, the energy of the system, ionization potentials (Koopmans' theorem), dipole moments, and wave functions that represent position and spin coordinates for the electrons in the molecular system. Based on a set of trial input geometry for a given molecule, the program will optimize the geometry through an energy-minimization procedure; this geometry optimization makes MNDO unique among methods in current use for large molecules. These calculations were performed using an IBM 3032 computer at Auburn University.

The input data used in this paper were first obtained from crystallographic data (Berman and Kim 1968). Actual coordinates for  $\beta$ -methyl glucopyranoside were not available, but  $\alpha$ -methyl glucopyranoside has been the subject of several studies. These data were modified slightly to account for the beta anomer and were used for the original trial coordinate system in this project.

The first step was to perform calculations on the ground state molecule, followed by each protonated form. Large differences in the energy of the ionic forms could indicate that one form is energetically favored over the other, and would perhaps be the preferred intermediate. Other computations were particularly concerned

TABLE 1. *Optimized geometry for beta-methyl glucopyranoside (I).*

Atom number I	Bond length (angstroms) IJ	Bond angle (degrees) IJK	Dihedral angle (degrees) IJKL	J	K	L
1						
2	1.5929			1		
3	1.5861	108.316		2	1	
4	1.5875	109.207	54.504	3	2	1
5	1.5856	110.929	307.208	4	3	2
6	1.5791	112.996	169.926	5	4	3
7	1.4081	110.545	304.434	1	2	3
8	1.3964	105.956	176.352	1	7	5
9	1.4006	121.867	196.121	8	1	2
10	1.1185	112.040	62.903	9	8	1
11	1.1157	113.504	300.217	9	8	1
12	1.1158	106.574	181.226	9	8	1
13	1.1348	110.008	66.456	1	2	3
14	1.3950	111.843	179.797	2	3	4
15	0.9473	113.315	281.753	14	2	3
16	1.1246	108.978	295.914	2	3	4
17	1.3960	107.130	185.212	3	4	5
18	0.9469	112.356	189.755	17	3	4
19	1.1263	109.183	66.103	3	4	5
20	1.3957	108.060	171.662	4	5	7
21	0.9473	111.935	155.213	20	4	5
22	1.1254	108.221	291.554	4	5	7
23	1.1219	109.945	58.961	6	5	7
24	1.1195	109.009	175.879	6	5	7
25	1.3921	112.705	293.668	6	5	7
26	0.9468	112.490	79.844	25	6	5
27	1.1260	110.154	64.124	5	7	1

with the charge and electron density at each atom in the system and the degree of bonding between individual atoms. Additionally, calculations were performed in which the proton was placed at a position approximately equidistant from the two oxygen atoms in question, and the geometry was allowed to optimize. It was assumed that the proton would gravitate towards the oxygen center through which the reaction occurs.

#### RESULTS AND DISCUSSION

As mentioned earlier, the question that is posed is concerned with the site of protonation. While experimental evidence currently indicates that the glycosidic oxygen is the most probable position at which the reaction occurs, results from this research give a less than conclusive picture.

Tables 1, 2, and 3 show the optimized geometry calculated for the ground state molecule (I), the protonation of the ring oxygen (II), and the protonation of the glycosidic oxygen (III), respectively. The bond lengths are reported in angstroms and represent the interatomic separation between atoms I and J, while the bond angle IJK is reported in degrees. The dihedral angle is the angle between vectors IJ and KL, in degrees, measured clockwise from K to J (see Fig. 3). The numbering system is as shown in Figs. 1 and 2.

TABLE 2. *Optimized geometry for structure II.*

Atom number I	Bond length (angstroms) IJ	Bond angle (degrees) IJK	Dihedral angle (degrees) IJKL	J	K	L
1						
2	1.5871			1		
3	1.5854	111.025		2	1	
4	1.5884	112.240	53.457	3	2	1
5	1.5851	112.517	308.013	4	3	2
6	1.5783	113.082	170.404	5	4	3
7	1.5272	106.730	308.753	1	2	3
8	1.3563	102.653	185.568	1	7	5
9	1.4173	129.046	20.791	8	1	2
10	1.1152	111.471	65.040	9	8	1
11	1.1128	112.375	301.370	9	8	1
12	1.1152	105.486	183.524	9	8	1
13	1.1313	112.030	63.469	1	2	3
14	1.3905	111.613	169.978	2	3	4
15	0.9490	112.980	445.623	14	2	3
16	1.1249	108.247	293.258	2	3	4
17	1.3935	108.877	188.971	3	4	5
18	0.9486	112.667	250.840	17	3	4
19	1.1250	108.175	67.541	3	4	5
20	1.3933	106.783	168.923	4	5	7
21	0.9487	112.726	135.928	20	4	5
22	1.1247	107.895	289.193	4	5	7
23	1.1218	110.465	67.859	6	5	7
24	1.1199	107.744	184.705	6	5	7
25	1.3921	108.576	306.302	6	5	7
26	0.9475	112.374	204.493	25	6	5
27	1.1244	107.243	62.952	5	7	1
28	0.9677	114.328	35.864	7	5	6

It can be seen in Fig. 4 that interatomic distances about the reaction center are changing in a manner that is at least qualitatively consistent with the two mechanisms in question. The bond length between C<sub>1</sub> and O<sub>7</sub> is lengthened by protonation of the oxygen within the ring and shortened by protonation of the glycosidic oxygen. The lengthening is as expected, since the proposed mechanism for the acyclic carbonium ion involves scission of this bond. Similarly, protonation of the O<sub>8</sub> position results in elongation of the C<sub>1</sub>—O<sub>8</sub> bond. This would be consistent with the loss of methanol to generate the cyclic carbonium ion. It is also interesting to note that protonation of this position results in a lengthening of the C<sub>9</sub>—O<sub>8</sub> bond, compared to the ground state.

From Table 4, it can be seen that the heats of formation and total energies of the structures are quite close to each other. Differences of this magnitude are not large enough to make a definitive choice between the two isomers. Lack of obvious differences at this point means that we must look to other sources of evidence in an attempt to elucidate the mechanistic pathway.

If we assume that the protonation reaction can be represented as an acid-base reaction, in which the proton is the acid, and the glucoside is the base, we should be able to assess the relative basicity of each oxygen, and therefore their reactivity

TABLE 3. *Optimized geometry for structure III.*

Atom number I	Bond length (angstroms) IJ	Bond angle (degrees) IJK	Dihedral angle (degrees) IJKL	J	K	L
1						
2	1.5878			1		
3	1.5882	108.212		2	1	
4	1.5925	110.824	50.313	3	2	1
5	1.5880	111.674	310.291	4	3	2
6	1.5729	114.139	167.944	5	4	3
7	1.3781	112.416	306.604	1	2	3
8	1.4883	103.654	177.235	1	7	5
9	1.4657	130.111	109.800	8	1	2
10	1.1121	109.323	70.054	9	8	1
11	1.1111	108.654	308.064	9	8	1
12	1.1141	106.044	189.613	9	8	1
13	1.1310	113.037	76.113	1	2	3
14	1.3908	114.479	168.015	2	3	4
15	0.9483	113.538	418.001	14	2	3
16	1.1264	108.432	291.715	2	3	4
17	1.3919	111.376	191.363	3	4	5
18	0.9484	112.650	275.984	17	3	4
19	1.1259	108.302	68.995	3	4	5
20	1.3934	109.034	167.827	4	5	7
21	0.9479	112.709	116.536	20	4	5
22	1.1241	108.202	289.661	4	5	7
23	1.1226	110.361	67.020	6	5	7
24	1.1211	108.024	183.298	6	5	7
25	1.3921	109.179	305.052	6	5	7
26	0.9476	111.746	200.423	25	6	5
27	1.1254	109.038	63.781	5	7	1
28	0.9634	113.239	270.706	8	1	2

toward the proton. To do this we must recall the concepts of Lewis and Bronsted Acid-Base Theory. In the Bronsted Theory, an acid is a proton donor, while a base is a proton acceptor. In the Lewis definition, an acid is a molecule which is electron-deficient; a base contains available electrons (Lowry and Richardson 1976). With these definitions in mind, we shall now examine the electronic structure of the glucoside ground state.

Table 5 contains a tabulation of the charge and electron density calculated for each atom in the  $\beta$ -methyl-glucopyranoside ground state. It is of interest that both the charge and electron density are greater at position O<sub>7</sub> (the ring oxygen) than at position O<sub>8</sub> (the glycosidic oxygen). This should indicate that the oxygen within the ring is more basic, according to the Lewis definition. Furthermore, these two

TABLE 4. *Heats of formation and total energy for each protonated form.*

Structure	$\Delta H_f$ (Kcal/mole)	Total energy (eV)
II	-86.56385	-3034.3212
III	-85.66299	-3034.2822

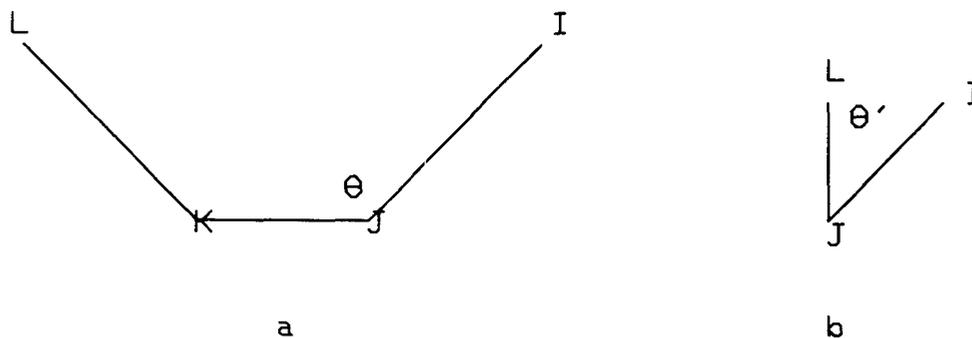


FIG. 3. Illustration of geometric dimensions reported in Tables 1, 2, and 3. a) I-J is bond length, and  $\theta$  represents the bond angle IJK. b) View along the JK axis showing that the dihedral angle ( $\theta'$ ) is the angle between vectors IJ and KL.

sites have a greater charge and electron density than any other oxygen in the molecule (atom numbers 14, 17, 20, and 25). Differences are also found to occur in the densities of the individual orbitals of the two oxygens in question (Table 6).

Upon protonation, the glycoside becomes a conjugate acid, and its strength as a Bronsted acid may be examined by the degree of bonding between the H-O<sub>7</sub>

TABLE 5. Charge and electron density for each atom in beta-methyl-glucopyranoside ground state.

Atom #	Charge	Electron density
1	0.2935	3.7065
2	0.0755	3.9245
3	0.0733	3.9267
4	0.1155	3.8845
5	0.1085	3.8915
6	0.1755	3.8245
7	-0.3614	6.3614
8	-0.3351	6.3351
9	0.2192	3.7808
10	-0.0264	1.0264
11	-0.0110	1.0110
12	0.0173	0.9827
13	-0.0057	1.0057
14	-0.3066	6.3066
15	0.1799	0.8201
16	0.0746	0.9254
17	-0.3186	6.3186
18	0.1944	0.8056
19	0.0075	0.9925
20	-0.3181	6.3181
21	0.1970	0.8030
22	0.0229	0.9771
23	-0.0037	1.0037
24	0.0370	0.9630
25	-0.3220	6.3220
26	0.1888	0.8112
27	0.0279	0.9721
	-0.0003	78.0003

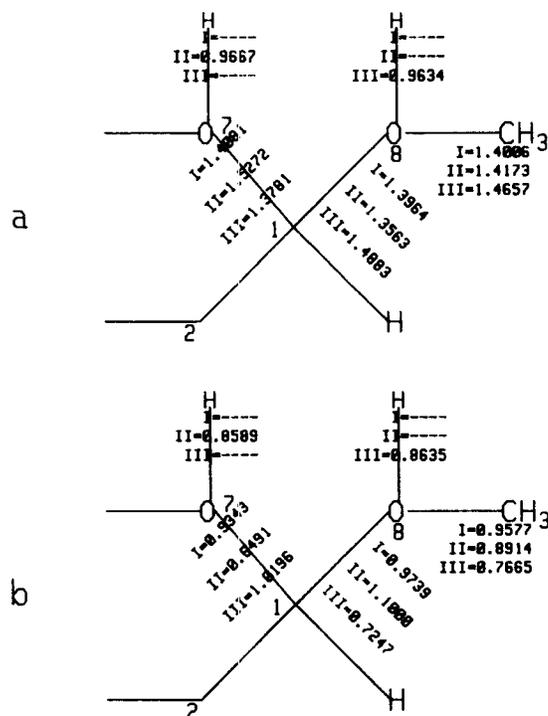


FIG. 4. Interatomic distances (a) and degree of bonding data (b) about the reaction center for structures I, II, and III.

and H—O<sub>8</sub> bonds. The values for the degree of bonding are an indicator of the strength and character of the linkage in question. Values approaching 1.0 would be indicative of a single bond, while values approaching 2.0 and 3.0 would mean that we are dealing with double and triple bonds, respectively. Higher values for the degree of bonding should indicate less tendency to dissociate, meaning that the equilibrium is shifted further to the right. It was found that the degree of bonding for structure III was 0.863492, while structure II was found to be 0.858889. This indicates that there should be a higher equilibrium concentration of the conjugate acid formed from the protonation of the glycosidic oxygen. It can be further noted (Fig. 4) that the degree of bonding about the reaction center mirrors the bond length results. Protonation of the ring oxygen (structure II) results in a large decrease in the degree of bonding between the C<sub>1</sub> and O<sub>7</sub> positions. Again this would follow, since the protonation of the O<sub>7</sub> position is postulated to involve an acyclic intermediate which is generated by the cleavage of this bond.

TABLE 6. Electron densities in each basis orbital for oxygens 7 and 8 in ground state.

Atom #	2S	Px	Py	Pz	Total
7	1.8241	1.7663	1.2420	1.5290	6.3614
8	1.8172	1.3362	1.3010	1.8807	6.3351

TABLE 7. Bond lengths and degree of bonding for proton placed between  $O_7$  and  $O_8$ , and allowed to optimize.

Bond	Initial bond length	Optimized bond length	Degree of bonding
$O_7-H_{28}$	1.277500	0.964136	0.849112
$O_8-H_{28}$	1.317187	2.327755	0.011198

Another interesting phenomenon that is observed involves the electron density about position number one. It has been assumed that the electron density at this position may alter the stability of the resultant carbonium ion (Bochkov and Zaikov 1979). Calculations performed in this study have indicated that structure II has a slightly higher electron density about this  $C_1$  position than does structure III.

Additionally, if we assume that the reaction does indeed proceed by protonation of the glycosidic oxygen, a question then arises with regard to the next step. Does the protonated form lose methanol to form the cyclic carbonium ion, or the methyl carbonium ion to produce the sugar directly? While it has been established with a fair degree of certainty that the actual mechanism occurs by way of the former pathway, degree of bonding data (Fig. 4) has shown that the bond between the methyl group and the oxygen is only slightly stronger than the bond between  $C_1$  and the glycosidic oxygen. Additionally, as was mentioned earlier, protonation at the  $O_8$  position results in a lengthening of the  $C_6-O_8$  bond length.

Results of the calculations in which the proton was placed in between positions  $O_7$  and  $O_8$  are shown in Table 7. It can be seen that after optimization, the proton is physically much closer to the  $O_7$  position, and also has a much greater degree of bonding in relation to the ring oxygen. Comparison of this information with that presented in Tables 2 and 3 shows close agreement with the results for structure II. Furthermore, these calculations confirm the greater Lewis basicity of the ring oxygen predicted by the charge and electron density results reported earlier.

Based strictly on energetic and electronic information, the actual mechanism of the reaction in question is still unclear. The results are varied between the two routes such that one method cannot be completely ruled out in favor of the other. In this regard, the information presented here is similar to the results of experimental analyses. There is no irrefutable evidence that the reaction occurs by a single method. It should be borne in mind, however, that the application of molecular orbital techniques to the chemical constituents of wood represents a largely unexplored area, such that the interpretation of results is still somewhat tentative, and may need revision as computations become more sophisticated.

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