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A Molecular Orbital Approach to the Effect of Acid and Base on Mutarotation of D-Glucose

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Synopsis. Molecular orbital calculations were performed for the study of the mechanism of the mutarotation of D-glucose (in Fig. 1) by the CNDO/2 method. The calculated results for a proposed mechanism are in good agreement with the experimental results in relation to the effect of the acid and the base, suggesting the validity of the proposed mechanism of mutarotation.

The mutarotation of D-glucose in solution is caused by the interconversion between α- and β-anomers. The mutarotation has been reported to be accelerated by acid or base, but this reaction is accelerated by the combination of both acid and base.[1,2] The proposed mechanisms of the acid, the base or the acid-base catalysis are shown in Fig. 1. All the three mechanisms include the formation of a chain intermediate by the cutting of the C_1–O_α bond. If we assume that the formation of this chain intermediate is the rate-determining step, it follows that if the acid or the base accelerates the breaking of the C_1–O_α bond, the reaction rate of the mutarotation should become faster on the whole. To investigate the validity of this interpretation, we performed a molecular orbital calculation by the CNDO/2 approximation,[3] and tried to inquire into the effect of the acid or the base.

Results and Discussion

The molecular structures of α- and β-D-glucose were determined by the energy gradient method in the CNDO/2 approximation using the program package GEOMIN.[4] The molecular structures thus obtained reproduced fairly well those obtained by the X-ray diffraction method.[5] In order to examine the effect of the acid and the base, we built models for the three mechanisms shown in Fig. 1. We chose H_3O^+ for the acid and H_2O, NH_3, OH^- for the base. The structures of the acid and the bases were optimized fully by the energy gradient method. H_3O^+ was set on the equatrial position of the ether oxygen(O_α) and the distance between the ether oxygen and the proton of H_3O^+ is 1.5 Å. The distance between the central atom of the bases and the proton of the anomeric OH group is also 1.5 Å. The central atom of the bases and this OH group were on a straight line. The conformation of the bases are as follows; the dihedral angle of C_1–O_β–O(base)–H′ equals to 90 degrees for H_2O and that of C_1–O_β–N(base)–H′ 180 degrees for NH_3. H′ stands for a proton of the bases. For OH^-, the proton of OH^- ion was set linearly. The position of the proton of the bases was determined so as to reduce the steric hindrance. We selected the arrangement of all atoms of the bases in this manner.

Furthermore, we define the symbols for special species; isolated glucose molecule is glucose^0, glucose interacting with H_3O^+ at the ether oxygen is glucose$^+$ and glucose^0 and glucose$^+$ interacting with the bases at the anomeric OH group are glucose^0-"base" and glucose$^+$-"base", respectively.

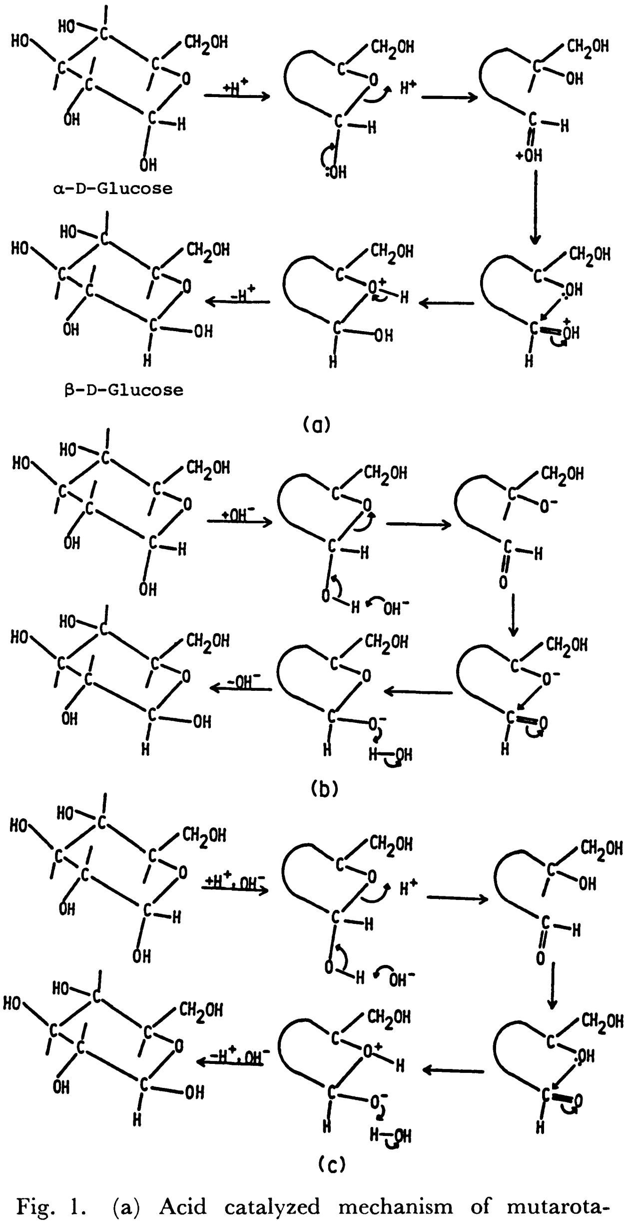

Fig. 1. (a) Acid catalyzed mechanism of mutarotation. (b) Base catalyzed mechanism of mutarotation. (c) Acid and base catalyzed mechanism of mutarotation.

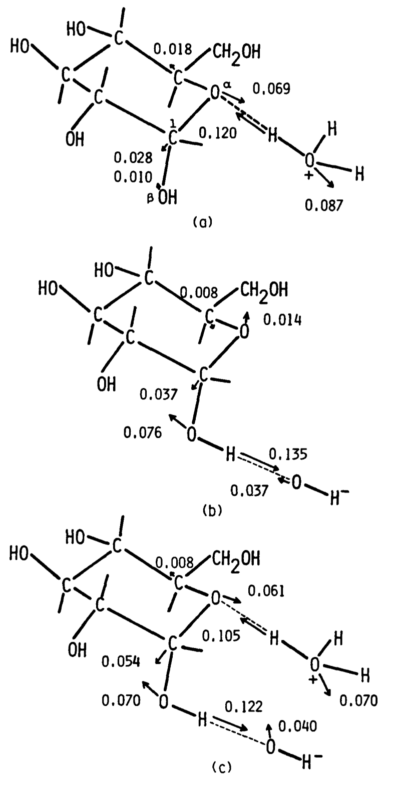

Fig. 2. Force on each atom for glucose$^+$ (a), glucose $-OH^-$ (b), and glucose$^+$ $-OH^-$ (c). Arrows in the figure represent the directions of forces, and numbers represent the magnitude of the forces in hartree/bohr.

Table 1. The Changes of Two Center Energies (E_{AB}) of C_1-O_α Bond (in kcal mol^{-1}) (α-form)

Species	E_{AB}	ΔE_{AB}[a]
Isolated form		
Glucose^0	−655.2	—
Acid catalysis		
Glucose$^+$	−640.3	15.0
Base catalysis		
Glucose^0-OH_2	−653.0	2.2
Glucose^0-NH_3	−652.3	2.9
Glucose^0-OH^-	−645.2	10.1
Acid-base catalysis		
Glucose$^+$-OH_2	−636.9	18.3
Glucose$^+$-NH_3	−635.7	19.5
Glucose$^+$-OH^-	−629.9	25.4

a) $\Delta E_{AB} = E_{AB}$(Species) $- E_{AB}$(Glucose^0).

Table 2. The Changes of Two Center Energies (E_{AB}) of C_1-O_α Bond when Anomeric Hydroxyl Proton is Extracted by Bases H_2O, NH_3, and OH^- (in kcal mol^{-1}) (α-form)

O-H bond length(Å)	H_2O	NH_3	OH^-
Glucose^0-"base" system[a,c]			
r_e	2.23	2.93	10.06
$r_e+0.1$	2.71	3.69	11.49
$r_e+0.2$	3.21	4.50	13.15
$r_e+0.3$	3.72	5.57	15.14
Glucose$^+$-"base" system[b,c]			
r_e	3.38	4.51	10.40
$r_e+0.1$	3.98	5.68	12.47
$r_e+0.2$	4.80	6.88	14.94
$r_e+0.3$	5.53	8.23	17.77

a) $\Delta E_{AB} = E_{AB}$(Glucose^0-"base") $- E_{AB}$(Glucose^0). b) $\Delta E_{AB} = E_{AB}$(Glucose$^+$-"base") $- E_{AB}$(Glucose$^+$). c) Optimized anomeric O_β-H bond length (r_e) is 1.032(Å).

For these models, the forces acting on the atoms were calculated by the energy gradient method. The results are shown in Fig. 2 for α-D-glucose. The common feature for the acid catalysis (a)(c) is that the force on the proton of H_3O^+ and that on the ether oxygen acts so as to attract each other and form a new O-H bond. As for the base catalysis (b)(c), the force on the proton of the anomeric OH group acts to elongate this O-H bond. Moreover it is noteworthy that the force to lengthen the C_1-O_α bond acts on both atoms and the C_1-O_β bond tends to shorten for all systems. These results are common to H_2O and NH_3. Needless to say glucose^0 has no component of force on each atom since its molecular structure was determined to be the equilibrium one by the energy gradient method.

In all model systems, the C_1-O_α bond was weakened by the interaction between glucose^0 and the acid or the base. The effects of the acid and the base were quantitatively evaluated by using the energy partition technique in the CNDO/2 method. The total energy (E) in the CNDO/2 method is represented in following form,

$$E = \sum_{A} E_A + \sum\sum_{A<B} E_{AB}$$

where E_A denotes the monoatomic contribution to the total energy of atom A, and E_{AB} the diatomic contribution of atoms A and B. The terms involved in E_A and E_{AB} were already evaluated in the literature[6] and hence are omitted here. The effects of the acid and the base were quantitatively evaluated by using the value of $E_{C_1\text{-}O_\alpha}$. That is, E_{AB} was regarded as a measure for the bond energy. In Table 1, the values of $E_{C_1\text{-}O_\alpha}$ are listed for α-D-glucose. This indicates that the C_1-O_α bond energy decreases in both glucose$^+$ and glucose^0-"base", and decreases much more in glucose$^+$-"base". These are in good agreement with the magnitude and the directions of the forces shown in Fig. 2. From these results, it is expected that the acid and the base increase the reaction rate for the mutarotation and the combination of the acid and the base increases the rate much more.

Next, on the supposition that the base abstracts the anomeric hydroxyl proton, $E_{C_1\text{-}O_\alpha}$ was calculated at three bond lengths of the O–H group. The differences in $E_{C1\text{-}O\alpha}$ between glucose^0 and glucose^0-"base" or between glucose$^+$ and glucose$^+$-"base" are respectively listed in Table 2 for α-D-glucose, indicating that the C_1–O_α bond energy decreases as the bond length of the O–H group increases. Moreover, the extent of the weakening of the C_1–O_α bond has relation to the strength of the base; OH^- remarkably decreases $E_{C1\text{-}O\alpha}$ followed by NH_3 and H_2O. The same results were obtained in β-D-glucose. That is, when the acid and the base interact with β-D-glucose, the forces on the atoms and the changes of the C_1–O_α bond energy have the same tendency as α-D-glucose.

Conclusion

We studied the effect of the acid or the base for the formation of a chain intermediate by analysis of both force and the C_1–O_α bond energy. From the results, we propose that the acid or the base facilitates the cleavage of the C_1–O_α bond and therefore speeds up the mutarotation as the whole. We also conclude that the acid-base catalysis increases the reaction rate more than the acid or the base catalysis alone and that the stronger the base the greater is the effect. Consequently, we can explain the experimental result by the present calculation and therefore suggest that the mechanism of the acid and the base catalysis in Fig. 1 is valid.

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