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Ab Initio Molecular Orbital Calculations on the Water–Carbon Dioxide System. Reaction Pathway for $H_2O + CO_2 \rightarrow H_2CO_3$

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Abstract: The reaction pathway for $H_2O + CO_2 \rightarrow H_2CO_3$ has been calculated using ab initio methods. The energy barrier was found to be 234 kJ/mol in the Hartree–Fock approximation with a basis set of double ζ quality. Correlation was accounted for by means of a configuration interaction calculation including singly and doubly excited configurations from the ground state. The inclusion of correlation effects lowered the energy barrier to 219 kJ/mol. The reaction was found to proceed with an attack of the oxygen atom in water on the carbon atom in carbon dioxide simultaneous with the proton transfer from the water to the carbon dioxide skeleton.

(I) Introduction

The formation of carbonic acid, H_2CO_3, and its associated ions, HCO_3^- and CO_3^{2-}, occurs through two different reaction mechanisms in aqueous solution.[2a] At neutral pH carbon dioxide reacts with water to form carbonic acid

$$H_2O + CO_2 \xrightarrow{k_1} H_2CO_3 \qquad (I)$$

which is in a fast equilibrium with the ionic species. In basic solution, pH >9.5, a hydroxide ion attacks carbon dioxide to form a bicarbonate ion directly

$$OH^- + CO_2 \xrightarrow{k_2} HCO_3^- \qquad (II)$$

Both these reactions require the rearrangement of covalent bonds and it is therefore perhaps not surprising that these reactions proceed with moderate rates ($k_1 = 0.03\ s^{-1}$ and $k_2 = 8.5\ s^{-1}\ mol^{-1}\ m^3$)[2a] at room temperature. The ionizations of

Table I. CPU Time on a UNIVAC 1108 for Different Parts of the Calculations on Carbonic Acid (C_s) and the Transition State

Type of calculation	CPU time, min
SCF calculation	20
Primary two-electron integrals	14
Construction of approximate natural orbitals	21
Transformation to molecular two-electron integrals	22
CI calculation	64
Total	141

H_2CO_3 into HCO_3^- and CO_3^{2-} are very rapid processes which are close to being diffusion controlled.[2b]

The transport of carbon dioxide in vertebrates is a complex process involving the hydration of dissolved CO_2 in the tissues and the dehydration in the lung capillary vessels. The hydration reaction I apparently would constitute a rate-limiting step in these processes. However, to speed up the hydration of carbon dioxide and the dehydration of carbonic acid, erythrocytes, for example, contain the enzyme carbonic anhydrase. This enzyme acts as a powerful catalyst with one of the highest turnover numbers known.[3] In spite of the fact that the three-dimensional structure of carbonic anhydrase is known to a resolution of about 2 Å,[3,4] the detailed catalytic mechanism of this enzyme is not understood.

In order to obtain a better understanding of the basic molecular interactions in the H_2O-CO_2 system we have performed a series of ab initio molecular orbital calculations. In the first two papers in the series we investigated the molecular complexes between H_2O and CO_2[5] and the heat of formation of carbonic acid.[6] In this paper we report a study of the reaction pathway for the hydration process I. These calculations are directly applicable only to the conditions in the gas phase but it is our belief that they might provide a basis from which both the enzymatic and nonenzymatic reaction may be understood.

Water–carbon dioxide is still a rather large system from a computational point of view and it is a formidable task to calculate an accurate potential energy hypersurface. We have for practical reasons reduced the number of degrees of freedom and also worked mainly within the Hartree–Fock approximation, although some correlation effects have been included in the final energy comparison. Nevertheless, the present calculation represents quite an extensive ab initio study of a bimolecular chemical reaction surface.

(II) Computational Details

The computations were performed using Gaussian atomic orbitals as basis functions. A moderately large basis set of double-ζ type was chosen with 7 s and 3 p primitive functions on oxygen and carbon[7] and 4 s and 1 p on hydrogen.[8] The functions were contracted to 4 s, 2 p and 2 s, 1 p, respectively. This choice yielded 78 primitive and 50 contracted basis functions. It would have been desirable to extend the uncontracted basis set and to include polarization functions on carbon and oxygen too, but the number of calculations needed to describe the potential energy hypersurface make this too costly.

The SCF calculations were performed with the program system MOLECULE,[9] which makes an extensive use of the molecular symmetry to reduce the computational effort. The configuration interaction (CI) calculations used the direct method as implemented in a new version of the MOLECULE-CI program system.[10] In this version the two-electron integrals over the atomic basis are calculated with the MOLECULE integral program in a symmetry adapted basis and are then transformed to a MO basis with explicit use of the symmetry also in the transformation step. For a system with C_s symmetry, as H_2CO_3 in this study, this reduces the transformation time to approximately one-half.

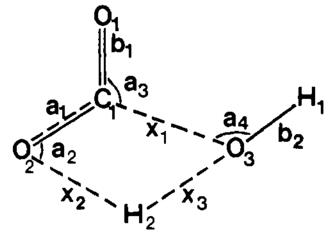

Figure 1. The reacting system. Labeling of atoms, bond distances, and bond angles.

An expansion of the wave function, including all single and double replacement states with respect to the approximate Hartree–Fock ground state, would with the present choice of basis functions result in an expansion comprising about 70 000 configuration state functions. This is substantially more than our computer can handle. The necessary truncation of the expansion was achieved in two ways. First the carbon and oxygen 1 s orbital and the corresponding virtual orbitals were excluded. Second, approximate natural orbitals were constructed from the remaining set of virtual canonical orbitals with the aid of first-order perturbation theory.[10] Out of the approximate natural orbitals only those with a occupation number larger than 2×10^{-3} were included in the final CI calculation. With the present basis set this limit has been shown to give approximately the same correlation energy difference as a full CI within 6 kJ/mol in a number of heat of reaction calculations.[11] The resulting wave function for H_2CO_3 in a $^1A'$ state of C_s symmetry then contains 12 810 nonzero terms. The timing data for the different steps in these calculations is found in Table I.

(III) The Search for a Transition State

A straightforward procedure in the calculation of a transition state is to compute the energy as a function of the geometrical parameters in a many dimensional grid. It is then possible to approximate these points with some analytical function and to find a stationary point of this function, in which the Hessian matrix (the matrix of second derivatives) contains one and only one negative eigenvalue. To do this without any further approximations for the reaction $H_2O + CO_2 \rightarrow H_2CO_3$ would mean the computation of an energy grid in 12 dimensions, which is impossible on any computer available today. To circumvent this problem we have introduced a number of approximations:

(a) The transition state was assumed to be planar. Certain support for this approximation is found in the second paper in this series,[6] where the equilibrium structure of H_2CO_3 was determined to be planar. The most stable molecular complex between H_2O and CO_2 is also planar.[5] A possible weakness of this approximation is that the HOH angle in the water molecule is made to increase more than it would do in a nonplanar transition state. However, the bending in water becomes flexible when one O–H bond is lengthened.[12]

(b) We have considered the formation of C_s symmetric H_2CO_3. In a previous calculation[6] it was found that the C_{2v} symmetric form has slightly lower energy than the C_s form. The interconversion between the C_{2v} and C_s forms should, however, not be the rate-determining step in the hydration of CO_2.

(c) The bond parameters b_1 and b_2 (Figure 1) are almost the same in reactants and product and it seems reasonable to

Table II. Second Derivatives of the Energy with Respect to the Independent Variables $\{x_i\}$ in the Saddle Point and the Corresponding Values in H_2CO_3

	$\partial^2E/\partial x_1^2$, N/m	$\partial^2E/\partial x_2^2$, N/m	$\partial^2E/\partial x_3^2$, N/m
Saddle point[a]	283	275	119
Carbonic acid	315	453	

[a] The eigenvalues of the Hessian matrix were −247, 411, and 513 N/m.

assume that they are not involved in the reaction to any large extent. These parameters were simply varied linearly as functions of a_1.

(d) To reduce the remaining seven degrees of freedom further we have chosen three independent variables, denoted by x_1–x_3 in Figure 1, and four dependent variables, a_1–a_4. That is, instead of computing an energy grid in seven dimensions we have considered it in three dimensions given by $\{x_i\}$ and for certain values of $\{x_i\}$ minimized the energy with respect to the parameters $\{a_i\}$.

(e) Minimizing the energy with respect to the four parameters $\{a_i\}$ means, in the valence force field approximation, at least nine calculations for a given value of $\{x_i\}$. To reduce the computational effort further the parameters $\{a_i\}$ were only optimized for ten different values of $\{x_i\}$. They were then fitted to second-order polynomials, $\{R_i\}$, in inverse powers of $\{x_i\}$

$$a_1 = A_1 + R_1(x_1,x_2,x_3) \qquad (1a)$$

$$a_i = A_i + B_i \arctan [R_i(x_1,x_2,x_3)] \qquad (1b)$$

$$i = 2, 3, 4$$

where the constants A_i and B_i are chosen to ensure the correct limiting behavior of the parameters $\{a_i\}$. With these approximations a three-dimensional energy grid was computed without optimizing the parameters $\{a_i\}$ for every value of $\{x_i\}$ but merely calculating them from eq 1a and 1b. This energy grid consisted of around 70 points with different values of $\{x_i\}$. Finally these points in the three-dimensional potential-energy surface were fitted to a fourth-order polynomial of inverse powers of $\{x_i\}$. In this surface a stationary point

$$E = P(x_1,x_2,x_3) \qquad (2)$$

which was a true saddle point, was located.

All the above calculations were made at the Hartree–Fock level of approximation. Correlation effects were only included in the three calculations on the reactants, the product, and the transition state.

(IV) Results

From the polynomial P, describing the energy as a function of $\{x_i\}$, a saddle point was obtained. The eigenvector of the Hessian matrix corresponding to the negative eigenvalue has a large contribution from all three of the independent variables $\{x_i\}$ as is typical for a concerted reaction. This can also be seen in the second derivatives $\{\partial^2E/\partial x_i^2\}$ shown in Table II, which are all positive although one of the eigenvalues of the Hessian matrix is negative. The geometry in the saddle point or transition state is shown in Figure 2.

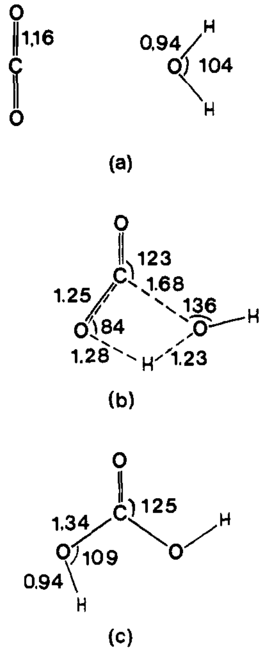

Figure 2. Optimized structures: (a) Water and carbon dioxide, (b) transition state, (c) carbonic acid. This structure is achieved by a 180° rotation of an OH bond around one of the C–O bonds in carbonic acid in its optimized C_{2v} structure (from ref 5 and 6). All distances in Å and angles in deg.

To establish that the saddle point found from the polynomial also was a true saddle point of the SCF energy surface, calculations were made along the eigenvectors of the Hessian matrix obtained from P. These calculations showed the correct behavior, that is, the curvature was negative along one eigenvector and positive along the eigenvectors corresponding to positive eigenvalues of the Hessian matrix. The saddle point of the SCF energy surface differed by less than 10 kJ/mol in energy and less than 0.04 Å in the variables $\{x_i\}$ from the one found from P. For computational reasons we used the saddle point obtained from the polynomial in the final CI calculation. The SCF calculation in this point gave the value 234 kJ/mol.

The correlation energy was found to be lower in the $H_2O + CO_2$ system than in H_2CO_3. This result may be attributed to the existence of a larger π system in CO_2 than in H_2CO_3. The energy barrier for the formation of H_2CO_3 decreased by 15 kJ/mol upon inclusion of correlation effects. For the reverse reaction the energy barrier decreased by 43 kJ/mol. The order of magnitude of these correlation effects is the same as those found in other calculations of energy barriers for reactions involving closed shell systems.[13]

The contribution to the correlation energy from higher excitations, E_{uc}, has also been accounted for in an approximate way, through the renormalization equation $E_{uc} = (1 - c_0^2)\cdot E_{corr}$ (see, for example, ref 14). E_{corr} is the correlation energy

Table III. Calculated Energies in Atomic Units and Normalization Constant for the CI Expansion for Reactants, Transition State, and Product

Molecules(s)	$-E_{SCF}$	$-E_{corr}$	$-E_{tot}$	c_0	$-E_{uc}$
$H_2O + CO_2$	263.2466	0.4045	263.6511	0.94720	0.0416
$[H_2CO_3]^\ddagger$	263.1577	0.4100	263.5677	0.94519	0.0437
H_2CO_3 (C_s)	263.2546	0.3937	263.6483	0.94978	0.0386
H_2CO_3 (C_{2v})	263.2582	0.3935	263.6517	0.94980	0.0385

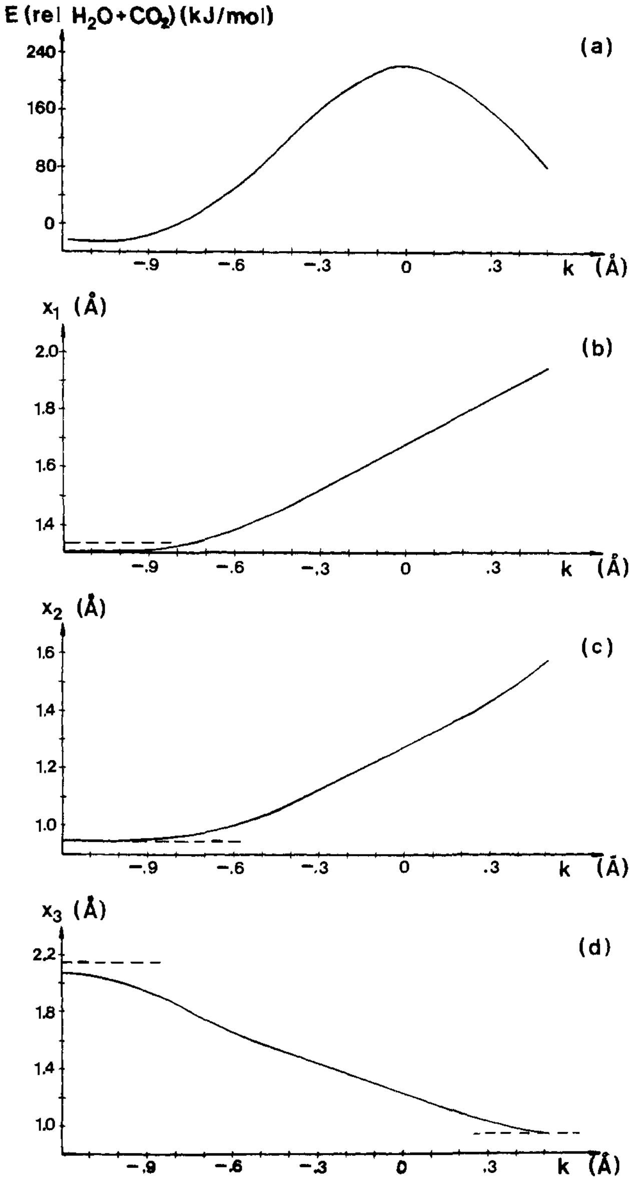

Figure 3. Variation of E and $\{x_i\}$ along the reaction pathway (E relative to $H_2O + CO_2$). The distance along the reaction pathway from the saddle point is denoted by k. The curves are terminated at $k = 0.5$ Å since the polynomial P is not valid for higher values of k. The dotted lines in (b)-(d) indicate equilibrium distances.

and c_0 is the coefficient for the approximate HF ground state in the normalized CI wave function. The inclusion of E_{uc} lowers the energy for the reactants and the transition state relative to carbonic acid (Table III). This effect is small and unimportant in the overall description of the system.

The terms "reaction coordinate", "reaction pathway", and "least energy pathway" are often used in the discussion of reaction surfaces without any clear definition. We prefer to use the word reaction pathway and to define it in accordance with Baskin et al.,[15] that is, starting from the found saddle point one goes in the two directions given by the eigenvector corresponding to the negative eigenvalue of the Hessian matrix. Away from the saddle point one goes in the direction of steepest descent. With this definition of the reaction pathway, which depends on the choice of coordinates,[16] it is then possible to describe how the three independent variables $\{x_i\}$ the parameters $\{a_i\}$ and the energy vary along the reaction pathway from reactants to product. In this case, however, it is not possible to describe the noninteracting reactants as the polynomial P is not valid for large x_1 and x_2. Figure 3 shows that the change in the variables $\{x_i\}$ is monotonic and simultaneous. In order to visualize the reaction we have drawn the structure of the reacting system at four positions along the reaction pathway in Figure 4.

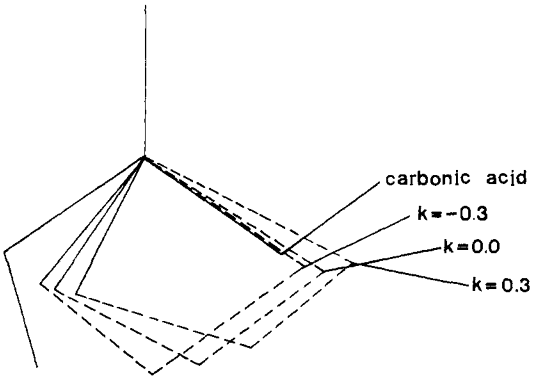

Figure 4. The reacting system at four positions along the reaction pathway. The dashed lines indicate bonds broken or formed.

Table IV. Energy Barriers for the Hydration and Dehydration Reaction with Different Wave Functions

	Energy barrier, kJ/mol	
	SCF wave function	CI wave function
$H_2O + CO_2 \rightarrow H_2CO_3$	234	219
$H_2CO_3(C_{2v}) \rightarrow H_2O + CO_2$	264	221

According to Hammond's postulate,[17] the transition state should resemble the reactants in an exothermic reaction and the products in an endothermic reaction. The hydration of CO_2 is an approximately athermic reaction, $\Delta E = -2$ kJ/mol, and consequently the transition state should be approximately midway between reactants and product. That this is the case is shown in Figure 2 and also in the overlap populations (Table V).

(V) Discussion

In the work of Baskin et al.[15] on the reaction $CH_2(^3B_1) + H_2 \rightarrow CH_3 + H$, it was shown that if the bond distance in the hydrogen molecule is chosen as an independent variable and the energy is minimized with respect to the others, one does not find the true saddle point. This is, for example, seen from the occurrence of discontinuities in the dependent variables. On the other hand, if the bond distance in the hydrogen molecule and the distance between one hydrogen atom in the hydrogen molecule and the carbon atom both are chosen as independent variables one will obtain a stationary point very close to the true saddle point.

In the hydration of CO_2 there are three bonds broken and formed and we have chosen all of them as independent variables, a procedure which we believe should be sufficient to avoid the pitfalls pointed out by Baskin et al. That this is the case is indicated by the smooth behavior of the variables $\{x_i\}$ and the energy along the reaction pathway (Figure 3).

The calculated value of the energy barrier is subject to several types of errors. The largest one is probably due to the incomplete basis set used. This error is present both on the SCF and CI level and we estimate it to 45 kJ/mol[11] including the error due to the truncation of the CI expansion already mentioned in section II. The error arising from the description of the energy hypersurface by a polynomial was found to be less than 10 kJ/mol through explicit calculations. It is more difficult to give a numerical estimate of the error caused by approximation (d) in section III. Since we should have avoided

Table V. Mulliken Population Analysis with SCF and CI Wave Functions for Reactants, Transition State, and Product[a]

		Gross atomic population						Overlap population						Dipole moment,
		C_1	O_1	O_2	O_3	H_1	H_2	C_1O_1	C_1O_2	C_1O_3	O_2H_2	O_3H_1	O_3H_2	D
H_2CO_3	SCF	4.972	8.539	8.454	8.492	0.765	0.777	1.136	0.522	0.477	0.623	0.633	0.010	3.57
	CI	4.994	8.529	8.446	8.483	0.768	0.780	1.077	0.482	0.438	0.608	0.618	0.010	3.53
$[H_2CO_3]^{\ddagger}$	SCF	4.985	8.489	8.628	8.560	0.758	0.580	1.116	0.654	0.295	0.349	0.663	0.294	3.54
	CI	5.003	8.482	8.618	8.548	0.761	0.587	1.050	0.602	0.277	0.343	0.641	0.286	3.51
$H_2O + CO_2$	SCF	5.112	8.444	8.444	8.275	0.862	0.862	1.157	1.157	0.0	0.0	0.675	0.675	2.11[b]
	CI	5.124	8.438	8.438	8.271	0.865	0.865	1.097	1.097	0.0	0.0	0.655	0.655	2.09[b]

[a] The numbering of the atoms refers to Figure 1. [b] The dipole moment of water.

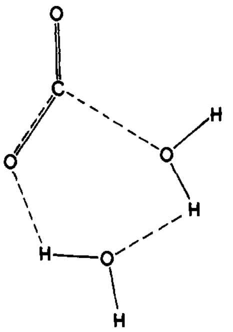

Figure 5. Possible transition state involving more than one water molecule.

the difficulties arising from the occurrence of several minima of the dependent parameters for a given value of the independent ones, comparison with the work of Baskin et al.[15] indicates that the error is relatively small.

The energy barrier for the reaction $H_2O + CO_2 \rightarrow H_2CO_3$ was determined to be 219 ± 55 kJ/mol (Table IV). This is much higher than the experimentally determined activation energy, 74 kJ/mol,[18] for the same reaction in aqueous solution.

The dipole moment of the activated complex is larger than for water (cf. Table V) which may mean that the activated complex is more stabilized in aqueous solution than is the reactants, that is, a lower activation energy is to be expected in aqueous solution than in the gas phase. The proton transfer from the water to the carbon dioxide skeleton is certainly facilitated by other water molecules, for the reaction occurring in the liquid phase (cf. Figure 5). This is probably the most important reason for the discrepancy between the computationally and experimentally determined energy barrier. Apart from the proton transfer a C═O double bond is broken and a C–O single bond is formed during the reaction. In Table V it is seen that the overlap populations for both these bonds have intermediate values in the transition state compared to the initial and final states. The energetics of changing these bonds is not in any obvious way affected by the presence of other water molecules. It is thus possible that the energy barrier for the reaction in aqueous solution is caused by the breaking and forming of these two bonds. The breaking of one of the carbon dioxide double bonds is also accompanied by a bending of the CO_2 molecule.

If the enzymatic reaction proceeds via a water molecule attack on the carbon dioxide, a part of the enzymatic mechanism may be to bind CO_2 and thereby facilitate the necessary deformation of the molecule. Although there are arguments against a strong binding of carbon dioxide to the enzyme,[19] such a mechanism is appealing. As is seen from the Mulliken population analysis, the charge on the oxygen atom O_2 increases from −8.438 in free CO_2 to −8.618 in the transition state and a CO_2 binding via the oxygen atom O_2 would stabilize this extra negative charge. The essential features of the enzymatic mechanism may also be an OH^--ion attack on carbon dioxide. The activation energy for this reaction, hydration reaction II, in aqueous solution is 55 kJ/mol.[20] In order to elucidate whether this barrier has its origin in the CO_2 deformation, thus supporting the above suggested enzymatic mechanism, or whether it is the result of the breaking of the hydration shell of OH^-, further work is now in progress in our laboratory.

Supplementary Material Available: Description of the polynomials R_i and P and a list of SCF calculations (5 pages). Ordering information is given on any current masthead page.

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