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Hydrogen-Bond Networks for Hydrolyses of Anhydrides

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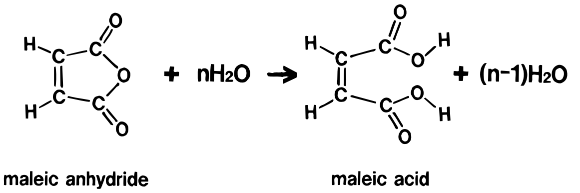
1. Introduction

The hydrolysis of anhydrides is an important reaction in organic chemistry. In spite of the accumulation of theoretical analyses of hydrolyses including ancillary water molecules ("a water-assisted mechanism"),[1−5] the following representative reactions are still unresolved.



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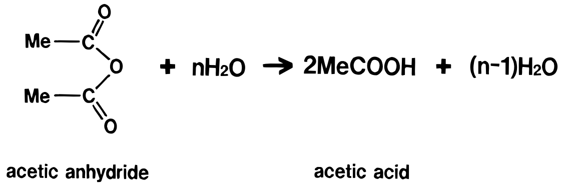

[2]

In general, for small *n* values, the hydration transition state (TS) is unfavorable due to nonlinear hydrogen-bond (H-bond) shapes. In contrast, for large *n* values, the lone-pair orbitals of oxygen cannot be directed toward the H−O bonds of other H_2O molecules, in spite of the apparently good H-bond linearity. It is therefore a mechanistic concern to find the optimal *n* values in these two hydrolyses.

In this study, reactions (1 and 2) are examined theoretically with various *n* values. Modeling of these reactions in aqueous media is very difficult. This difficulty arises from there being only a vague distinction between reactant and solvent water molecules through rapid proton transfer. These reactions (1 and 2) will therefore be dealt with in the gas phase (substrate anhydrides and water clusters).

The computed results are expected to shed some light on solvation and the possible proton relay of the hydrolysis in a neutral environment (pH = 7). Even in the gas phase, it seems to be informative to investigate the hydrogen-bond networks during hydrolysis. It will be shown that the optimal *n* value for reaction 1 is different from that for reaction 2.

2. Method of Calculation

RHF/6-31G* geometry optimizations, analyses of vibrational frequencies, and subsequent single-point calculations of MP3/6-31G* have been carried out to evaluate the Gibbs free energies of reactions 1 and 2. To check the electron-correlation effect, the Becke3lyp/6-31G* [6] TS geometry optimizations of reactions 1 and 2 were also performed with their respective optimal *n* values. Computations have been made using the Gaussian 94 program[7] on the CONVEX SPP-1200/XA computer (Information Processing Center in Nara University of Education).

3. Results of Calculations and Discussions

Figure 1a shows three hydrolyses of reaction 1. For $n = 1$, 2, and 3, the lone-pair orbitals of nucleophilic water molecules approach the carbonyl carbon atoms in the direction of the $\pi^*_{C=O}$ orbitals (the state A). As the reactions proceed, the cyclic TS shapes are formed. Hydrogen bonds in the $n = 3$ TS are less strained than those in the $n = 1$ and 2 TSs. The $n = 3$ TS geometry shows that a nucleophile, a proton donor, and an ancillary water molecule are needed for the facile proton transfer to occur. It is noteworthy that there is a difference in the positions of the black-circle protons in $n = 1$, 2, and 3 of product complexes, B's. In $n = 1$ and 2, bent and small networks are produced inside of the hydroxy groups. In $n = 3$, linear and large networks occur outside hydroxy group. The constraint of planarity due to the vinyl group in the maleic anhydride requires a large ($n = 3$) hydrogen-bond network for hydrolysis. There is a zwitterionic structure in the $n = 3$ TS. A hydronium ion like species is generated and its non-network hydrogen atom is protonic (0.51). At the same time, the carboxylate oxygen atoms are anionic (−0.68 and −0.77). H_3O^+ and CO^- moieties are involved, which are subject to a large solvent effect and consequently to a greater degree of stabilization. The reasonable hydrogen-bond network of the $n = 3$ TS can be tested by the other method, becke3lyp/6-31G*. Although the hydrogen-bond distances (in particular, 1.49−1.27 Å) are varied, the overall features of the $n = 3$ TSs are similar. That is, strainless cyclic hydrogen-bond networks are formed by two methods. Table 1 shows changes of in the Gibbs free energies. Energies of the reactant-like complexes (A's) are taken as standards. In line with the linearity of the hydrogen-bond geometries shown in Figure 1, the $n = 3$ $\Delta G^‡$ value is the smallest one. As a gas-phase reaction, the enthalpy energy barrier of $n = 3$, + 30.64 kcal/mol, is reasonable, although it would be lowered significantly by the solvation to the TS (H_3O^+ and CO^- zwitterionic character).

The $n = 4$ routes of reaction 1 have been examined by the use of various initial geometries. All of the attempts, however, have failed in obtaining the hydrolysis pathway.

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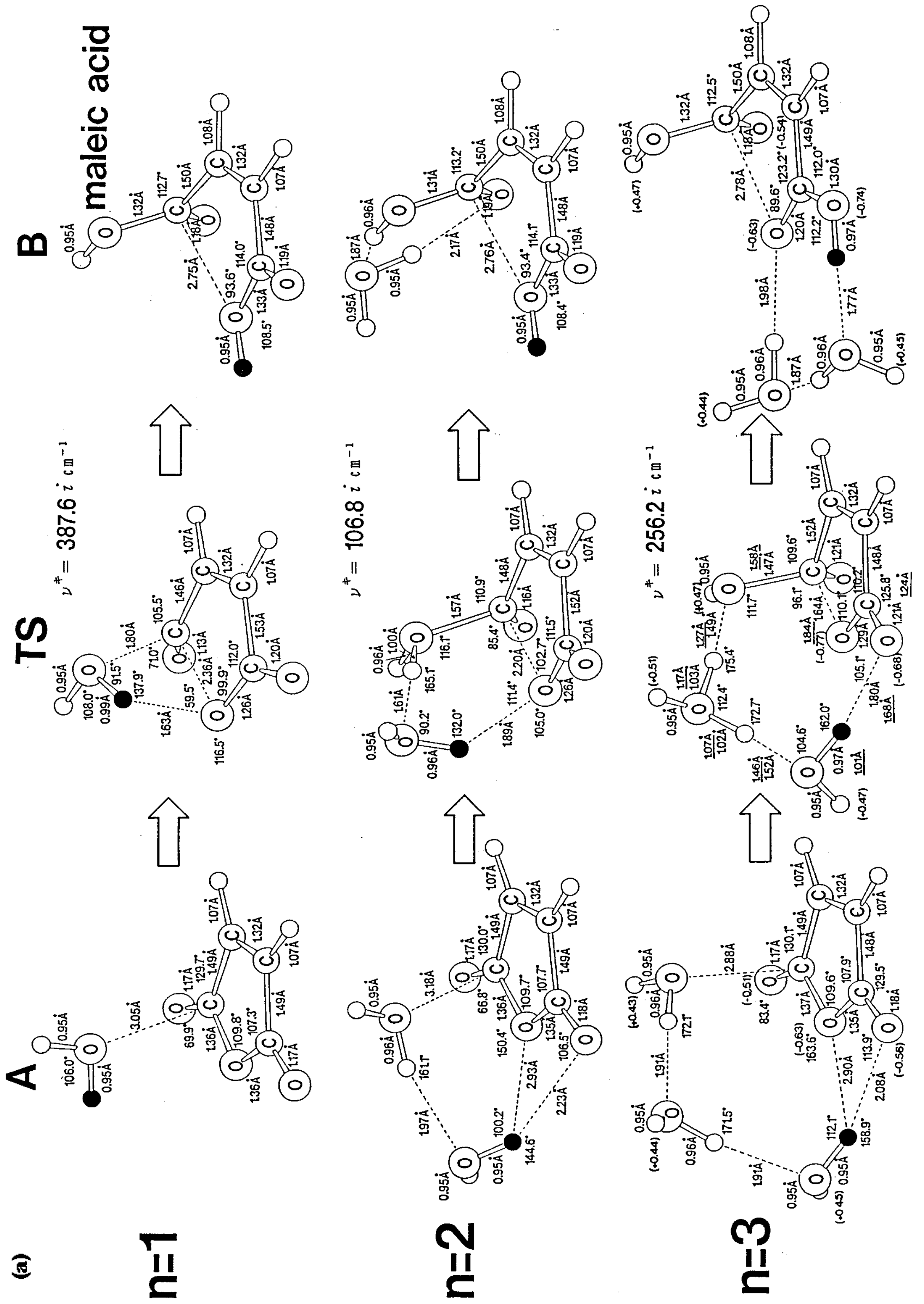

(a)
n=1
n=2
n=3
A
TS
B
maleic acid
ν‡ = 387.6 i cm⁻¹
ν‡ = 106.8 i cm⁻¹
ν‡ = 256.2 i cm⁻¹

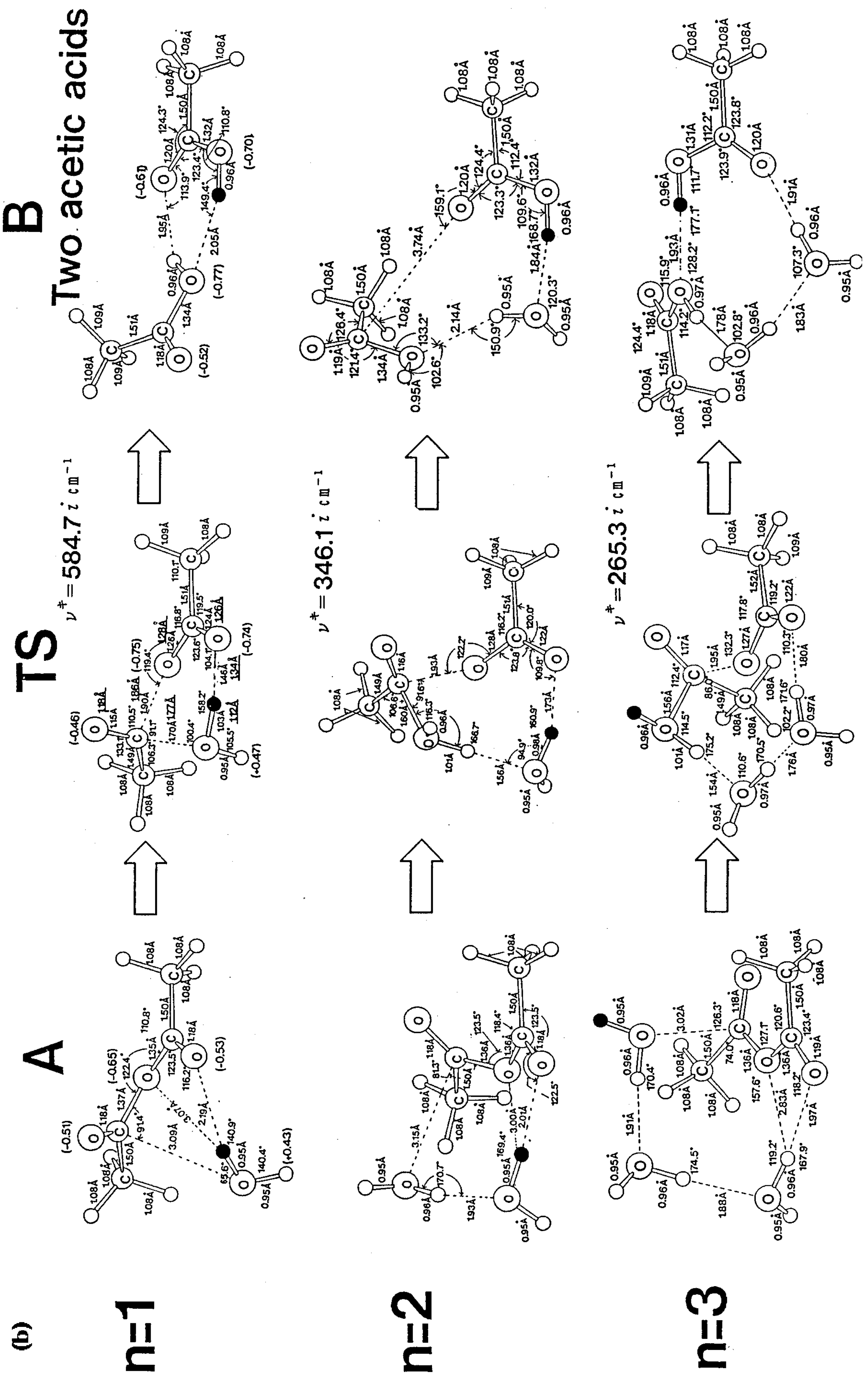


Figure 1. RHF/6-31G* geometries of three stationary points, A, TS, and B, of three hydrolyses between (a) maleic anhydride and water molecules (reaction 1) and (b) acetic anhydride and water molecules (reaction 2). Empty circles stand for hydrogen atoms, and black ones denote protons bound in the carboxyl groups of the state B. At the TS, the sole imaginary frequencies, $\nu^{\ddagger}$s, are shown. At the $n = 3$ TS of (a) and the $n = 1$ TS of (b), Becke3lyp/6-31G* distances are shown as underlined numbers. In parentheses, atomic net electronic charges (positive, cationic) are exhibited.

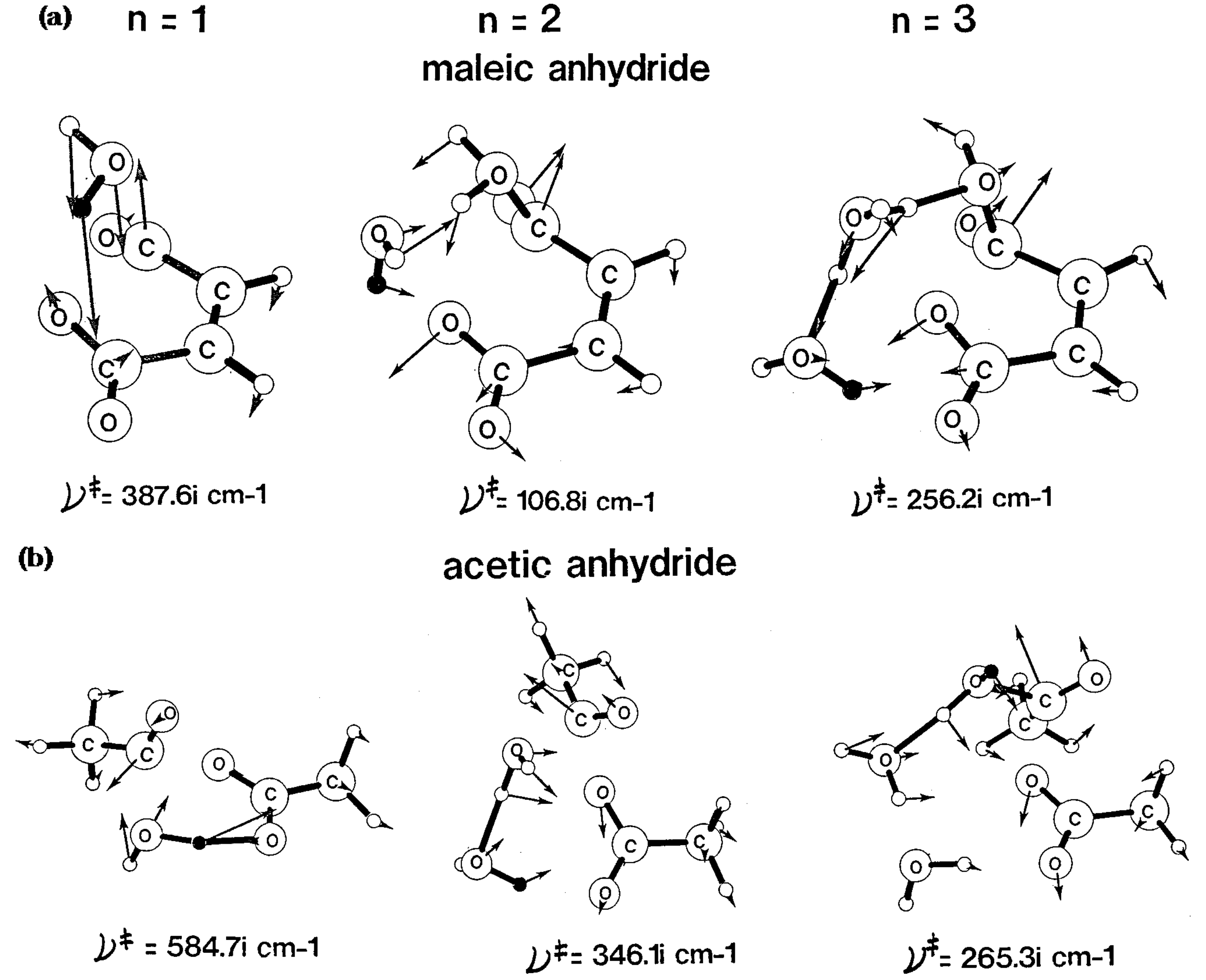


Figure 2. Reaction-coordinate vectors corresponding to sole imaginary frequencies of hydrolyses of (a) maleic anhydride and (b) acetic anhydride.

Table 1. Changes of Gibbs Free Energies (in kcal/mol) Relative to Those of Reactant-like Complexes (A's)

nH$_2$O		A, precursor	TS	B, product-like complex	nH$_2$O		A, precursor	TS	B, product-like complex
		Reaction 1 (Figure 1a)					Reaction 2 (Figure 1b)		
$n = 1$	ΔG	0	51.70	−2.27	$n = 1$	ΔG	0	34.82	−11.30
	ΔH	0	47.68	−4.95		ΔH	0	31.19	−11.37
	$-T\Delta S$	0	4.02	2.68		$-T\Delta S$	0	3.63	0.07
$n = 2$	ΔG	0	45.37	−4.58	$n = 2$	ΔG	0	38.04	−14.44
	ΔH	0	41.72	−5.51		ΔH	0	33.97	−12.97
	$-T\Delta S$	0	3.65	0.93		$-T\Delta S$	0	4.07	−1.47
$n = 3$	ΔG	0	37.75	−6.89	$n = 3$	ΔG	0	37.61	−15.27
	ΔH	0	30.64	−8.88		ΔH	0	33.19	−14.32
	$-T\Delta S$	0	7.11	1.99		$-T\Delta S$	0	4.42	−0.95

[a] Electronic total energies are evaluated by a single-point calculation of the third-order Møller−Plesset perturbation with the 6-31G* basis set on the RHF/6-31G* geometry (MP3/6-31G*//RHF/6-31G*). Thermal correction and entropy values are of RHF/6-31G* ($T = 298$ K, $P = 1$ atm).

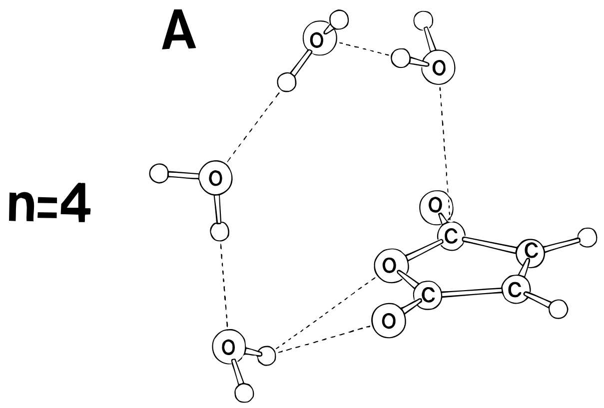
Some models are transformed into the $n = 3$ TS and an outer H$_2$O molecule. A reasonable pathway should have a strain-free hydrogen-bond circuit in the weakly bound complex, A. The $n = 3$ A (Figure 1a) is a prototype.

A model A of $n = 4$ is constructed (Scheme 1), where the O− − −O and C− − −O distances are set to 3 Å. The resulting tetramer cannot fit the constrained geometry of maleic anhydride for ready proton transfer. Thus, the water trimer (and, of course, the trimer fragment in the tetramer and pentamer) is the reagent of hydrolysis for maleic anhydride (in the gas phase).

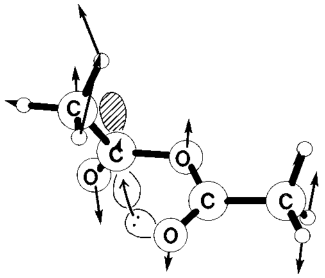
Figure 2a exhibits reaction coordinates at three TS's. Their vector movements indicate that the three TS geometries in Figure 1 are really saddle points. At $n = 3$, proton-relay and C−O bond-cleavage modes are noticeable.

Figure 1b shows the geometric changes in the three hydrolyses of acetic anhydride (reaction 2). Three reactant-like complexes, A's, are compared. The $n = 3$ A geometry involves a planar anhydride moiety. At $n = 1$ and 2 A geometries, the anhydride moieties are distorted. The free ($n = 0$) molecule has a nonplanar geometry due

Scheme 1. A Model $n = 4$ Hydrogen-Bond Network for Reaction 1

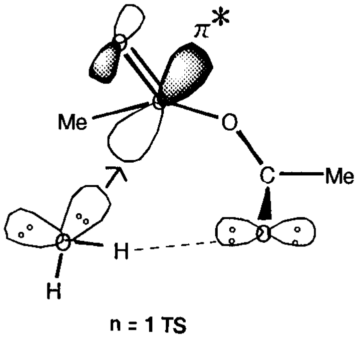


Scheme 2. Geometry of Acetic Anhydride and Its Facile Internal Rotation along the Low-Frequency (47.2 cm^{-1}) Vibration

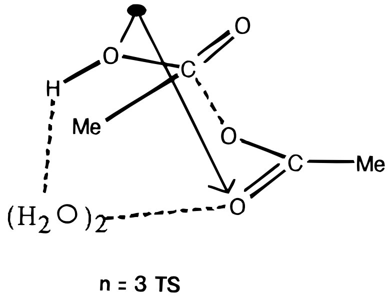


to an internal charge transfer (Scheme 2). Acetic anhydride is, by nature, flexibly distortable at the lowest frequency (47.2 cm^{-1}) rotational mode. The hydrogen-bond networks of A's ($n = 1$, 2, and 3) are all strain free due to the flexibility of the molecule. Even the $n = 1$ A has a reasonable geometry for bond interchanges (Scheme 3). There appears to be no need to further examine the $n = 2$ and 3 models because the geometric changes for A, TS, and B of $n = 1$ are reasonable. The black-circle protons are shifted smoothly from the water molecules to the carboxylate sites. But in the $n = 3$ model, the black proton moves peculiarly. This movement is verified in the reaction-coordinate vectors shown in Figure 2b. Scheme 4 has also been confirmed by IRC calculations.[8] Thus, the $n = 3$ geometry can almost be said to be composed of $n = 1$ plus a water dimer. The water trimer cannot react with acetic anhydride. This is flexible, in contrast with maleic anhydride, which is without flexibility. Table 1b shows the changes in the Gibbs free energies. The $n = 1$ free-energy barrier is found to be the smallest one of the three structures.

Scheme 3. A Charge-Transfer Interaction Assisted by a Hydrogen Bond



Scheme 4. During the TS Proton Migration, the $n = 3$ Mode Exists Almost as an $n = 1$ Structure Linked with a Water Dimer



The geometric flexibility of acetic anhydride requires no auxiliary water molecules for its hydrolysis. A water molecule is the reactant.

For the $n = 1$ TS, the solvation sites are carboxylate oxygen atoms and the carbon atom in the "acylium ion, $CH_3C^+{=}O$". The carboxylate sites cause strong outer hydrogen bonds. The acylium carbon atom may cause coordination bonds with the outer H_2O molecules.

Maleic anhydride undergoes hydrolysis with the water-trimer cluster. However, the hydrolysis of acetic anhydride proceeds with a single water molecule. The presence or absence of ring constraint in substrates makes a crucial difference in the bond interchanges during hydrolysis. Therefore, phthalic anhydride will need the H_2O trimer, whereas benzoic anhydride requires the monomer for hydrolysis.

Supporting Information Available: Cartesian coordinates of optimized geometries in Figure 1 (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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