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# A Theoretical Study of the Effect of a Tetraalkylammonium Counterion on the Hydrogen Bond Strength in *Z*-Hydrogen Maleate

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**Abstract:** High-level ab initio calculations (B3LYP/6-31+G** and QCISD(T)/6-311+G**) were carried out to resolve the disagreement between recent experimental and computational estimates of the relative strength of the intramolecular hydrogen bond in *Z*-hydrogen maleate anion with respect to the normal hydrogen bond in maleic acid. The computational estimates for the strength of the intramolecular hydrogen bond in the gas-phase maleate anion are in a range of 14−28 kcal/mol depending on the choice of the reference structure. Computational data suggest that the electrostatic influence of a counterion such as a tetraalkylammonium cation can considerably weaken the hydrogen bonding interaction (by 1.5−2 times) in the complexed hydrogen maleate anion relative to that in the naked anion. The estimated internal H-bonding energies for a series of Z-maleate/$R_4N^+$ salts (R = $CH_3$, $C_2H_5$, $CH_3CH_2CH_2CH_2$) range from 8 to 13 kcal/mol. The calculated energy differences between the *E*- and Z-hydrogen maleates complexed to $Me_4N^+$, $Et_4N^+$, and $Bu_4N^+$ cation are 4.9 (B3LYP/6-31+G(d,p)) and 5.7 and 5.8 kcal/mol (B3LYP/6-31G(d)). It is also demonstrated that the sodium cation exerts a similar electrostatic influence on the hydrogen bond strength in bifluoride anion ($FHF^-$). The present study shows that while low-barrier short hydrogen bonds can exist in the gas phase (the barrier for the hydrogen transfer in maleate anion is only 0.2 kcal/mol at the QCISD(T)/6-311+G**//QCISD/6-31+G** level), whether they can also be strong in condensed media or not depends on how their interactions with their immediate environment affect their strength.

## 1. Introduction

Short-strong hydrogen bonds (SSHB) have recently attracted attention because of their possible role in enzymatic processes.[1] Cleland, Kreevoy, and Frey et al.[2] have suggested that low-barrier hydrogen bonds (LBHB) can supply up to 20 kcal/mol in an enzyme-catalyzed reaction. Opposing views have been presented.[3] The requirements typically proposed for forming such LBHBs are the presence of a fairly strong acid in the absence of hydrogen bonding or a polar solvent such as water and similar $pK_a$ values of the two heteroatoms involved in the hydrogen bond. Almost all low-barrier hydrogen bonds involve charged systems and are most typically formed through short-strong hydrogen bonds. Although there are a variety of SSHB in both the gas and solid phase, as determined also by X-ray crystallography,[4a] this does not necessarily require that short H-bonds are strong. Interactions between neutral partners do not typically exceed 10 kcal/mol and cannot be made stronger by compressing the donor/acceptor distance.[4c] There have been numerous experimental and theoretical studies designed to measure the hydrogen bond strength in such model systems as *Z*-hydrogen maleate. NMR data indicate that strong, intramolecular H-bonds can exist in aqueous−acetone solutions of hydrogen maleate.[2c] However, recent NMR studies have shown that the characteristic downfield-shifted signal in aprotic solvents was observed in all cases independent of whether intra- or intermolecular hydrogen bonds were involved.[2d] In the present study we provide theoretical evidence that a tetraalkylammonium counterion markedly influences the strength of intramolecular hydrogen bonds.

**(a) Experimental Studies.** Schwartz and Drueckhammer[4d] have measured the effects of solvent on hydrogen bond donor and acceptor capability on the relative strengths of normal hydrogen bonds exemplified by neutral diacids and the low-barrier hydrogen bonds of their corresponding monoanions. They have experimentally measured the equilibrium constant for catalyzed (thiophenyl radical, thiourea) *E*/*Z* isomerization equilibria of such unsaturated diacids and monoanions as maleic/fumaric (Scheme 1, R = H) and citraconic/mesaconic acids (R = $CH_3$). The counterion chosen was a tetraalkylammonium salt and it was suggested that ion pair interactions would not be relevant since the steric bulk of a quaternary *n*-butylammonium salt would be sufficient to preclude an intimate ion pairing of the $R_4N^+$ and the carboxylate anion. It is also typically assumed that the nitrogen atom in $R_4N^+$ is positively charged. However,

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(1) (a) Gerlt, J. A.; Kozarich, J. W.; Keynon, G. L.; Gassman, P. G. *J. Am. Chem. Soc.* **1991**, *113*, 9667. (b) Kenyon, G. L.; Gerlt, J. A.; Petsko, G. A.; Kozarich, J. W. *Acc. Chem. Res.* **1995**, *28*, 178.

(2) (a) Cleland, W. W.; Kreevoy, M. M. *Science* **1995**, *269*, 104. (b) Frey, P. A. *Science* **1995**, *269*, 104. (c) Lin, J.; Frey, P. A. *J. Am. Chem. Soc.* **2000**, *122*, 11258. (d) Bruck, A.; McCoy, L. L.; Kilway, K. V. *Org. Lett.* **2000**, *2* (14), 2007.

(3) (a) Warshel, A.; Papazyan, A.; Kollman P. A. *Science* **1995**, *269*, 102. (b) Warshel, A.; Papazyan, A. *Proc. Natl. Acad. Sci. U.S.A* **1996**, *93*, 13665. (c) Shan, S.-O.; Herschlag, D. *J. Am. Chem. Soc.* **1996**, *118*, 5515. (d) Shan, S.-O.; Herschlag, D. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, *93*, 14474. (e) Shan, S.-O.; Stewart, S.; Herschlag, D. *Science* **1996**, *272*, 97.

(4) (a) For a discussion see: Guthrie, P. *Chem. Biol.* **1996**, *3*, 163. (b) Guthrie, J. P.; Kluger, R. *J. Am. Chem. Soc.* **1993**, *115*, 11569. (c) Scheiner, S.; Kar T. *J. Am. Chem. Soc.* **1995**, *117*, 6970. (d) Schwartz, B.; Drueckhammer, D. G. *J. Am. Chem. Soc.* **1995**, *117*, 11902. (e) Smallwood, C. J.; McAllister, M. A. *J. Am. Chem. Soc.* **1997**, *119*, 11277. (f) Pan, Y.; McAllister, M. A. *J. Org. Chem.* **1997**, *62*, 8171. (g) Pan, Y.; McAllister, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 166. (h) Kumar, G. A.; McAllister, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 3159.

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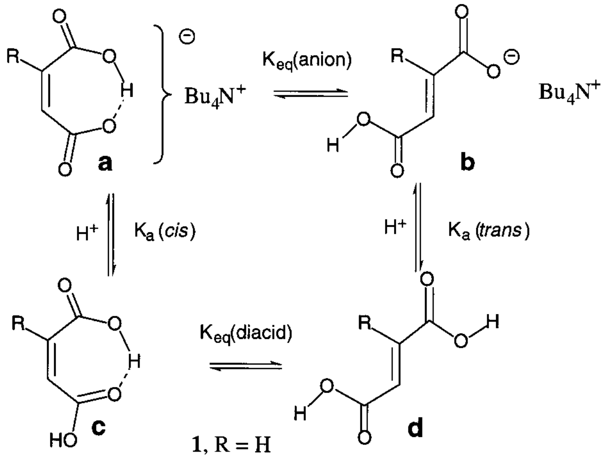
**Scheme 1**



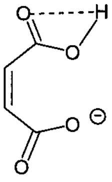
**1**, R = H
**2**, R = $CH_3$

this is a *formal charge* on the nitrogen atom that is used for "electron book keeping" and as such should not be used for estimating the *actual charge distribution* in molecules.

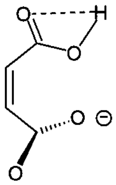
Within this *E*/*Z* model system (Scheme 1) the *difference* in relative free energies of the equilibrating *E*- and *Z*-isomers is used to provide an estimate of the *relative* strengths of the intramolecular hydrogen bond formed by the *Z*-anions (**1a** and **2a**) versus the normal hydrogen bonds in the diacids (**1c** and **2c**). These equilibration experiments[4d] showed that the diacids favor the *E*-isomer in all solvents studied; the monoanions also favored the *E*-isomer in protic solvents such as water and methanol. However, the *Z*-isomers of the monoanions that formed LBHB were greatly favored in such aprotic solvents as DMSO and $CHCl_3$. In protic solvents such as $CH_3OH$ the $K_{eq}$ values were quite similar ($\Delta\Delta G = 0.7 \pm 0.1$ and $1.0 \pm 0.1$ kcal/mol for maleate anion/maleic acid and citraconic/mesaconic anions/diacids, respectively).[4d] The relative H-bond strength became stronger in an aprotic solvent such as DMSO ($\Delta\Delta G = 4.4 \pm 0.2$ kcal/mol for citraconic/mesaconic anions/diacids). In general, the lower the solvent polarity the stronger the hydrogen bond.

In the presence of a tetrabutylammonium cation, the hydrogen bond in the monoanion of citraconic acid in $CHCl_3$ solvent was estimated to be 5.5 kcal/mol stronger, in terms of Gibbs free energy, than the normal hydrogen bond in the neutral diacid. It was suggested that this value must be a *lower* limit for the relative hydrogen bond strength in these monoanions vs a normal H-bond.[4d] However, since it is now known[2d] that hydrogen fumerate also engages in intermolecular H-bonding in aprotic solvents, this free energy difference must also include the difference between intra- versus intermolecular H-bonding in this equilibrating *E*/*Z* system. NMR experiments of Perrin[5] using the method of isotopic perturbation of equilibrium suggest that a pair of equilibrating tautomers exists in both aqueous and organic solvents.[5b] The asymmetry was attributed to disordered H-bonding in aqueous solution and to a counterion effect in nonpolar media.

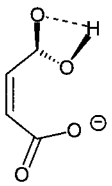
**(b) Theoretical Studies.** Cleland and Kreevoy have defined a hydrogen bond in an enzyme, where the heavy atom geometry is adjusted so that the enzyme can perform its catalytic function, as the increase in Gibbs free energy that would occur if the hydrogen bond were deleted.[2a] McAllister utilized this concept to estimate the H-bond strength in maleate anion with the planar anti *Z*-isomer **3a** where the hydrogen is rotated away from the internal oxygen atom. The *Z*-configuration of maleate anion, which lacks the intramolecular hydrogen bond between the $CO_2^-$ and COOH fragments, was used as the reference structure.[6a,7] The gas-phase hydrogen bond strength in the hydrogen maleate monoanion was considered to be the difference in energy (27.82 kcal/mol, B3LYP/6-31+G(d,p)) between isomers **1a** and **3a**.[6a] Approximating the solvent as a dielectric continuum reduces the calculated H-bond strength by about 6 kcal/mol at all levels of theory supporting the contention that for all cavity polarity values the ionic LBHB are significantly stronger than conventional H-bonds.[4g] Scheiner and Kar[4c] also used ab initio calculations to test the SSHB hypothesis and arrived at the conclusion that the requisite amount of energy is not available in neutral hydrogen bonds and that no additional energy may be derived from shortening such a H-bond.



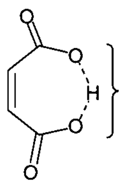
**3a**



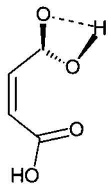
**3b**



**3c**



**3d**



**4**

Lluch et al.[8a] have suggested that the free energy difference between the monoanions of maleic (**1a**) and fumaric (**1b**) acids was 14.14 kcal/mol (MP2/6-31+G**). The gas-phase LBHB in **1a** was estimated to be 18.35 kcal/mol ($\Delta\Delta G = 20.43$ kcal/mol) stronger than the corresponding normal H-bond in the neutral diacid (**1c**). This value is also much higher than the experimental estimate.[4d] This apparent discrepancy between experiment and both computational studies,[6,8] leading to an estimated hydrogen bond strength of 21 kcal/mol even in a polar solvent, was attributed to the competing effects of the strong intramolecular H-bond and the destabilizing effect of forming a *Z*-double bond. Since the experiments[4d] were carried out in solution as monotetrabutylammonium salts, a question arises as to whether ion-pair interactions can affect the hydrogen bond strength estimates in the condensed phase relative to those of gas-phase monoanions and acids. Indeed, the experiments do suggest ion-pair interactions in such nonpolar solvents as benzene although these seem to be lacking in chloroform and DMSO solutions.[5b] To address the question of the electrostatic influence of a counterion, we carried out calculations that examined the magnitude of the intramolecular hydrogen bonding interactions of tetramethyl-, tetraethyl-, and tetra-*n*-butylammonium cations with maleate anions and compared these results with data for the naked gas-phase *Z*-maleate anions.

## 2. Computational Methods

Ab initio molecular orbital calculations[9] were performed with the Gaussian 94 and 98 system of programs.[10] The Becke three-parameter hybrid functional[11a,12a] combined with the Lee, Yang, and Parr (LYP) correlation functional,[11b] denoted B3LYP,[12b] was employed in the

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(5) (a) Perrin, C. L. *Science* **1995**, *266*, 1665. (b) For a detailed discussion see: Perrin, C. L.; Nielson, J. B. *J. Am. Chem. Soc.* **1997**, *119*, 12734.

(6) (a) McAllister, M. A. *Can. J. Chem.* **1997**, *75*, 1195. (b) Chen, J.; McAllister, M. A.; Lee, J. K.; Houk, K. N. *J. Org. Chem.* **1998**, *63*, 4611 and references therein.

(7) Structures **3a**−**c** have an intramolecular H-bond within the COOH fragment itself and the energy difference between **3b** and **1a** gives a *relative* strength of the H-bond in **1a** vs that in **3b**.

(8) (a) Garcia-Viloca, M.; Gonzalez-Lafont, A.; Lluch, J. M. *J. Am. Chem. Soc.* **1997**, *119*, 1081. (b) Garcia-Viloca, M.; Gonzalez-Lafont, A.; Lluch, J. M. *J. Phys. Chem. A* **1997**, *101*, 3880.

(9) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

**Table 1.** Relative Energies[a] of Various Configurations of Maleate Anion and a Transition Structure for Hydrogen Transfer

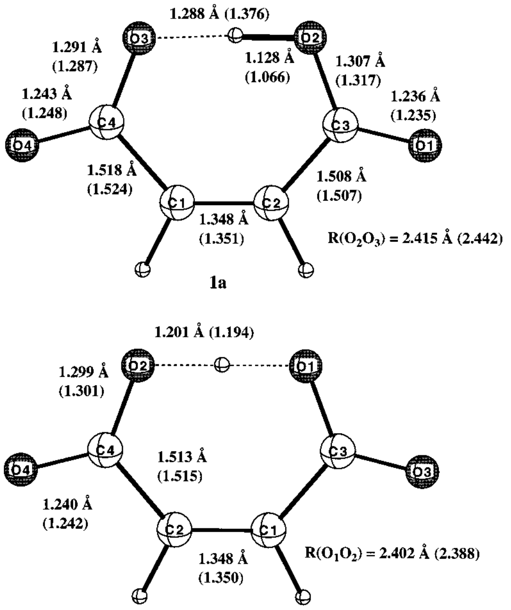
| structures | $\Delta E$ B3LYP/6-31+G** | $\Delta G$(298 K) B3LYP/6-31+G** | $\Delta E$ COSMO/6-31+G**//B3LYP/6-31+G** |
|---|---|---|---|
| *Z*-maleate anion **1a** | 0 | 0 | 0 |
| *E*-maleate anion **1b** | 14.6 (15.7)[b] | 14.6 | 1.1[e], 6.7[f] |
| *Z*-maleate anion (planar)[c] **3a** | 26.7 (27.9)[b] | | |
| *Z*-maleate anion **3b** | 19.5 (20.6)[b] | 19.7 | |
| *Z*-maleate anion ($CO_2H$ twisted) **3c** | 23.4 (24.4)[b] | | |
| *Z*-maleate anion, TS **3d** | 0.02[d] (−0.8)[b] | | |

[a] In kcal/mol. [b] $\Delta E$ + ZPE(B3LYP/6-31+G**) values are given in parentheses. [c] A second-order saddle point. [d] The $\Delta E$ value is 0.1 kcal/mol at the QCISD(T)/6-311+G**//B3LYP/6-31+G** level. The QCISD(T)/6-311+G**//QCISD/6-31+G** calculations lead to the $\Delta E$ value of 0.2 kcal/mol. Incorporating the ZPE(B3LYP/6-31+G**) corrections results in a negative adiabatic potential energy barrier of −0.7 kcal/mol. See refs 8 and 9a for a discussion of the physical sense of such a negative barrier. [e] In $CH_3OH$ (see ref 17). [f] In $CHCl_3$.

calculations using density functional theory (DFT). Geometries were optimized[13] at the B3LYP and QCISD (for **1a** and **3d**) levels using the 6-31+G** basis set. Structures involving the larger tetraethyl and tetra-*n*-butylammonium ions were optimized at the B3LYP/6-31G* level. The relative energies of **1a** and **3d** were refined by single point calculations at the QCISD(T)/6-311+G** level of theory. The stationary points on the potential energy surfaces were characterized by calculations of vibrational frequencies at the B3LYP/6-31+G** level. Zero point energies (ZPE) computed at the B3LYP/6-31+G** level were scaled by 0.9806.[14] Corrections for solvation were made using the polarizable conductor COSMO model and SCIPCM model reaction field calculations.[15] Throughout the text, bond lengths are in angstroms and bond angles are in degrees.

## 3. Results and Discussion

**Relative Energies of Various Configurations of Maleic and Fumaric Monoanions and Their Diacids. (a) Activation Barrier for Proton Transfer in *Z*-Hydrogen Maleate.** The calculated barrier for intramolecular proton transfer in *Z*-maleate anion **1a** is extremely small; and the calculated zero point vibrational energy available to the system is known to be as large as the barrier height for the proton transfer at both the MP2 and B3LYP levels of theory.[5b,6,8] Our primary objective is simply to ensure that at higher levels of theory the proton transfer is also barrierless. A transition structure (TS-**3d**, Figure 1) for the proton transfer in *Z*-maleate anion **1a** has 0.02 and 0.10 kcal/mol higher energy than **3b** at the B3LYP/6-31+G** and QCISD(T)/6-311+G**//B3LYP/6-31+G** levels of theory. The barrier for the hydrogen transfer in maleate anion **1a** is slightly larger at the higher level of theory (0.2 kcal/mol at the QCISD(T)/6-311+G**//QCISD/6-31+G** level). The main point is that the adiabatic potential energy barrier (with ZPE) is negative at all levels of theory employed including QCISD(T). However, when the classical barriers are this small, the ZPE derived from a harmonic vibrational calculation has to be taken with caution. This intramolecular hydrogen bond is strong in the gas phase and also has a low barrier (Table 1). Such an H-bond clearly qualifies as a LBHB and to the extent that it is also associated with a short O···O bond distance (2.39 Å) it may also be classified as a SSHB.



**1a**

**TS-3d**

**Figure 1.** Selected geometrical characteristics of *Z*-maleate anion **1a** and a transition structure **3d** for the hydrogen transfer in **1a** optimized at the B3LYP/6-31+G** and QCISD/6-31+G** (in parentheses) levels. Their relative energies are given in Table 1; total energies are given in Table S1 (Supporting Information).

**(b) Reference Structures for Estimating Relative H-Bond Strength.** One measure of the strength of a hydrogen bond is the difference between the energies of a structure containing an H-bond and a reference structure that differs from the structure in question only by the absence of that hydrogen bond. The difference in energy between these structures is governed not only by the hydrogen bond energy but also other factors.[6b,8] For example, the neutral *E*-diacid **1d** is 3.6 kcal/mol (3.3 kcal/mol at B3LYP/6-31+G(d,p)) lower in energy than its *Z*-isomer **1c** *despite the absence of the intramolecular H-bond in the former.* A configuration of maleic acid with a COOH group rotated about 90° (**4**) (Figure 3) is also a minimum albeit it is 3.9 kcal/mol higher in energy than maleic acid **1c** (Table 2). The *Z*-configuration of maleate anion with a perpendicular

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(10) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(11) (a) Becke, A. D. *Phys. Rev. A* **1988**, *37*, 785. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev.* **1988**, *B41*, 785.

(12) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Stevens, P. J.; Devlin, F. J.; Chablowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *80*, 11623.

(13) (a) Schlegel, H. B. *J. Comput. Chem.* **1982**, *3*, 214. (b) Schlegel, H. B. *Adv. Chem. Phys.* **1987**, *67*, 249. (c) Schlegel, H. B. In *Modern Electronic Structure Theory*; Yarkony, D. R., Ed.; World Scientific: Singapore, 1995; p 459.

(14) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502.

(15) (a) Barone, V.; Cossi, M.; Tomasi, J. *J. Comput. Chem.* **1998**, *19*, 404. (b) Foresman, J. B.; Keith, T. A.; Wiberg, K. B.; Snoonian, J.; Frisch, M. J. *J. Phys. Chem.* **1996**, *100*, 16098.

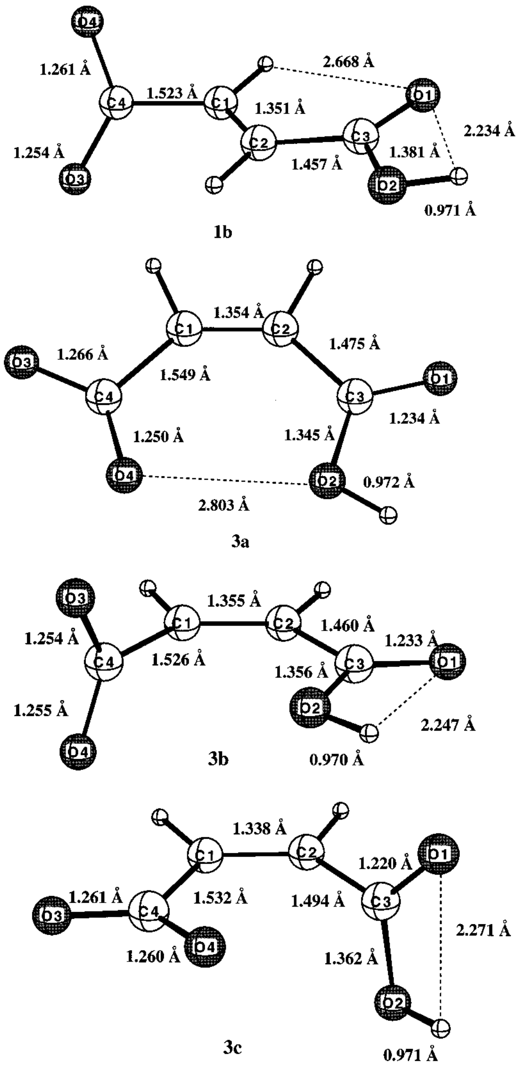

**Figure 2.** Selected geometrical characteristics of low-energy conformations of maleate and fumaric monoacid anions optimized at the B3LYP/6-31+G** level. Their relative energies are given in Table 1.

orientation of its neutral COOH fragment is a minimum (**3c**) (Figure 2) although it lies 3.9 kcal/mol higher in energy than **3b** (Table 1). The steric influence of two *Z*-COOH groups on a carbon−carbon double bond is of the same magnitude as the hydrogen bond in the neutral *Z*-maleic acid and this is a definite disadvantage of this *E*/*Z* model system.

*Z*-Maleate anions such as **3a** and **3b** have been used to calculate the intramolecular hydrogen bonding strengths in these ionic molecules. In particular, the planar $C_s$ structure of *Z*-maleate anion, without a hydrogen bond (**3a**),[6] has been used as a reference compound. However, since this is a second-order saddle point (two imaginary frequencies) nonplanar structure **3b**, with its carboxylate anion fragment rotated by ca. 90°, is the minimum reference compound that we have used. Relative to nonplanar *Z*-monoanion, the strength of the hydrogen bond in **1a** is estimated to be 19.7 kcal/mol ($\Delta\Delta G$ value, Table 1). The relative strength of this ionic hydrogen bond with respect to the strength of the normal hydrogen bond in neutral maleic acid (estimated as the difference between the energies of **1c** and **4**) is $\Delta\Delta G = 17.2$ kcal/mol.

Using *E*-monoanion **1b** as a reference structure gives a relative strength of the hydrogen bond in **1a**, with respect to the normal hydrogen bond in neutral maleic acid **1c** (the energy difference between **1c** and **1d**) of 17.9 kcal/mol (19.3 kcal/mol with ZPE); the energy difference −3.3 kcal/mol (−3.6 kcal/mol with ZPE) between **1c** and **1d** is also included (Figure 4). The free energy difference ($\Delta\Delta G$) for this H-bonding interaction ((**1b** − **1a**) + (**1c** − **1d**)) is 17.1 kcal/mol at the B3LYP/6-31+G** level (Tables 1 and 2).[16]

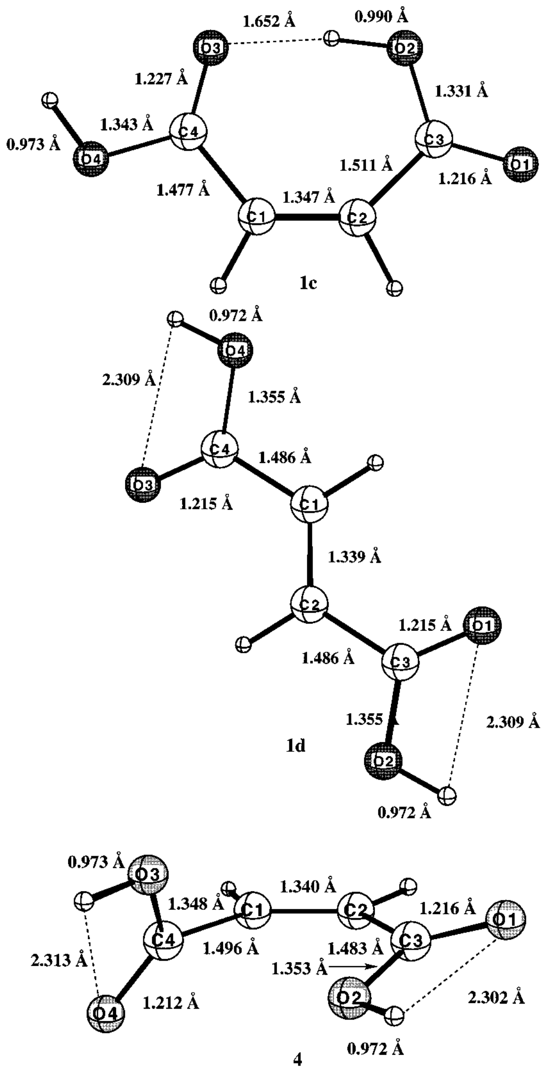

**Figure 3.** Low-energy conformations of maleate and fumaric monoacids optimized at the B3LYP/6-31+G** level. Their relative energies are given in Table 2.

**Table 2.** Relative Energies[a] of Maleic and Fumaric Acids in the Gas Phase and in Methanol

| structures | $\Delta E$ maleic acid **1c**/ fumaric acid **1d** | $\Delta E$ maleic acid **1c**/ twisted maleic acid **4** |
|---|---|---|
| B3LYP/6-31+G** | 3.3 (3.6)[b,c] | −3.9 (−3.3)[b,d] |
| SCIPCM//B3LYP/6-31+G** | 2.0 | −3.9[e] |

[a] In kcal/mol. [b] $\Delta E$ + ZPE(B3LYP/6-31+G**) values are given in parentheses. [c] The $\Delta G$(298 K) value is 2.5 kcal/mol. [d] The $\Delta G$(298 K) value is −3.9 kcal/mol.

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(16) Using **1b** as a reference structure implicitly assumes that the stabilization energies of the E-linkage of conjugated double bonds vs the Z one are almost the same for monoanions **1a** and **1b** and for the diacids **1c** and **1d** and that these energies cancel each other. In fact, they are different ($\Delta\Delta G$ values are 5.1 and 3.9 kcal/mol, respectively; estimated as $\Delta\Delta G$ energy differences between **1b** and **3b**, as well as **1c** and **4**) (Tables 1 and 2). By contrast, the experimental energy difference arising from the interaction of two methyl groups on a C═C (*E*- and *Z*-2-butenes) is <1 kcal/mol.

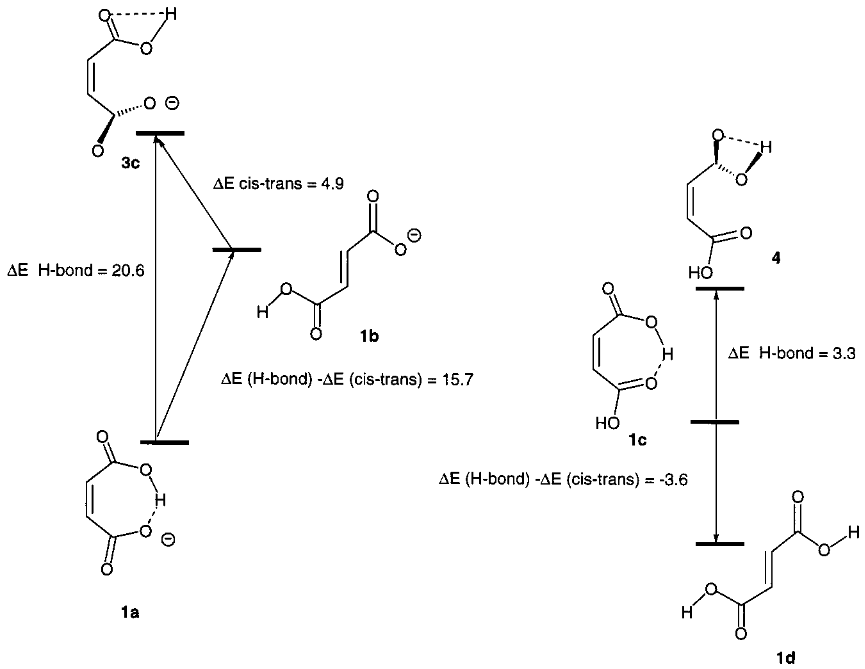

**Figure 4.** Estimates of the relative H-bond strength based on relative stabilities of various conformations of maleic and fumaric acids as well as of their monoanions. The energies (kcal/mol) calculated at the B3LYP/6-31+G** + ZPE(B3LYP/6-31+G**) level are shown.

In methanol solvent, the relative energy of the *E*-monoanion **1b** is only 1.1 kcal/mol with respect to **1a** due to a stronger stabilization of more polar *E*-monoanion (Table 1)[17] which is quite close to the experimental estimate[4d] of 0.7 ± 0.1 kcal/mol for the $\Delta\Delta G$ value (in favor of the *E*-monoanion).

Another measure of the normal internal H-bond in neutral maleic acid **1c** may be estimated by simply rotating the interacting hydrogen away as in **4** ($\Delta E = 3.3$ kcal/mol, Table 2; the relative energies of **1c**, **1d**, and **4** are not significantly changed by solvent). In the absence of this H-bonding interaction the *Z*-arrangement of the two COOH groups relative to neutral *E*-isomer **1d** is 6.9 kcal/mol higher in energy (the energy difference between **1d** and **4**; Figure 4).[16] However, the *Z*-monoanion of maleic acid **1a**, *as a consequence of a strong ionic hydrogen bond*, is 15.7 kcal/mol more stable than its *E*-isomer **1b.** With the above approaches we have bracketed the internal ionic hydrogen bonding strength of *Z*-hydrogen maleate to be between 16 and 20 kcal/mol.

**Counterion Effect.** When the theoretical gas-phase H-bond strengths differ significantly from experimental data, the validity of using a naked gas-phase anion to estimate the H-bonding strength, in the absence of the obligatory counterion, is brought into question. Since the experiments[4d] were carried out for mono-tetrabutylammonium salts, we need to measure the effect of the ion-pair interactions on the hydrogen bond strength in the condensed phase relative to the gas-phase monoanions and acids. To address the question of the electrostatic influence of a counterion, we carried out a series of calculations using tetraalkylammonium cations as the counterion and compared these results with data for the naked gas-phase anions.

Here, we describe two approaches for the estimation of the internal H-bonding energy in these overall neutral salt complexes. These calculations mirror those above in studies on maleate anion itself. The first method is based upon the sum of energy differences between *E*- and *Z*-maleate complexes (*E*/*Z* approach) and the energetic contribution due to structural changes from *E*- to *Z*-geometry of the central double bond (compare **1c** and **1d**, Figure 4 and Table 2). The second approach involves relative energies of the complexes with conformers of *Z*-maleate with and without the internal H-bonding interaction with the carboxylate (structures **3a**, **3b**, and **3c**, Figure 2). We have not examined intermolecular H-bonding interactions.[2d]

**Complexation with Tetramethylammonium Cation.** The electrostatic impact of a positively charged counterion on the H-bond strength of a maleate monoanion should be quite large. The magnitude of the proton affinity (PA) of hydrogen maleate **1a** (321.2 kcal/mol) estimated at the B3LYP/6-31+G** level speaks to the fact that dissociation of RCOOH to a naked carboxylate anion and a proton is attended by a significant increase in energy. Neutral ionic complex **5a** (Figure 5) formed between intramolecularly hydrogen bonded **1a** and a tetramethylammonium cation has a stabilization energy of −103.7 kcal/mol relative to its isolated reactants. The intramolecular hydrogen bond distance to the carboxylate oxygen ($H-O_3$) in neutral complex **5a** is significantly longer (1.490 Å, Figure 5) than it is in monoanion **1a** (1.288 Å). This indicates a weakening of the H-bond in *Z*-maleate through the complexation with the tetramethylammonium cation.

The more basic, higher energy ($\Delta E = 14.6$ kcal/mol, Table 1) *E*-monoanion **1b** is complexed more strongly than **1a** with $Me_4N^+$ and the stabilization energy for this isomeric complex **5b** is −117.5 kcal/mol due to the stronger intermolecular H-bonds ($C-H\cdots O$) in this complex. The hydrogen bonds formed by carboxylate oxygen atom ($O_3$) with the methyl hydrogens are weaker in **5a** (2.122 and 2.098 Å) than those in complexes **5b** (2.056 and 2.059 Å) and **5c** (2.106 and 2.040 Å) that have larger stabilization energies (Table 3). Furthermore, the hydrogen bonds between the $O_4$ oxygen atom and the methyl hydrogens in **5b** (1.926 Å) and **5c** (1.941 Å) are shorter than that in **5a** (1.974 Å) (Figure 5).[18] The distance between the $O_2$ and $O_3$ atoms in **5a** is 2.511 Å (Figure 5) whereas it is shorter

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[17] We used methanol for solvent effect modeling since when the dielectric constant approaches that of methanol there is a leveling effect and no further decrease in energy is observed.[6] According to SCIPCM calculations, in methanol solvent, the *E*-monoanion **1b** is 9.7 kcal/mol higher in energy than **1a**, which is far beyond the experimental estimate.[4d] The total energies from COSMO and SCIPCM solvent calculations are given in the Supporting Information (Table S1).

**Table 3.** Relative Energies[a] of Various Configurations[b] of a Complex of Maleate Anion with Tetramethylammonium Cation

| complexes | $\Delta E$ B3LYP/6-31+G** | $\Delta G$(298 K) B3LYP/6-31+G** | $\Delta E$ COSMO// B3LYP/6-31+G** |
|---|---|---|---|
| *Z*-maleate + Me$_4$N$^+$ **5a** | 0 | 0 | 0 |
| *E*-maleate + Me$_4$N$^+$ **5b** | 5.1 (4.9)[c] | 4.3 | 1.1[d], 4.4[e] |
| *Z*-maleate, CO$_2^-$ twisted + Me$_4$N$^+$ **5c** | 10.7 (10.2)[c] | 9.3 | |
| *Z*-maleate, CO$_2$H twisted + Me4N$^+$ **5d** | 11.9 (11.4)[c] | 11.2 | |

[a] In kcal/mol. [b] Shown in Figure 1 except **5d**. [c] $\Delta E$ + ZPE(B3LYP/6-31+G**) values are given in parentheses. [d] In CH$_3$OH; the relative energy of **5b** vs **5a** according SCIPCM calculations is 7.2 kcal/mol due to a larger stabilization of the *Z*-monoanion in methanol, which is counterintuitive and could be due to problems with cavity definition for molecules of this size (see ref 6b). [e] In CHCl$_3$.

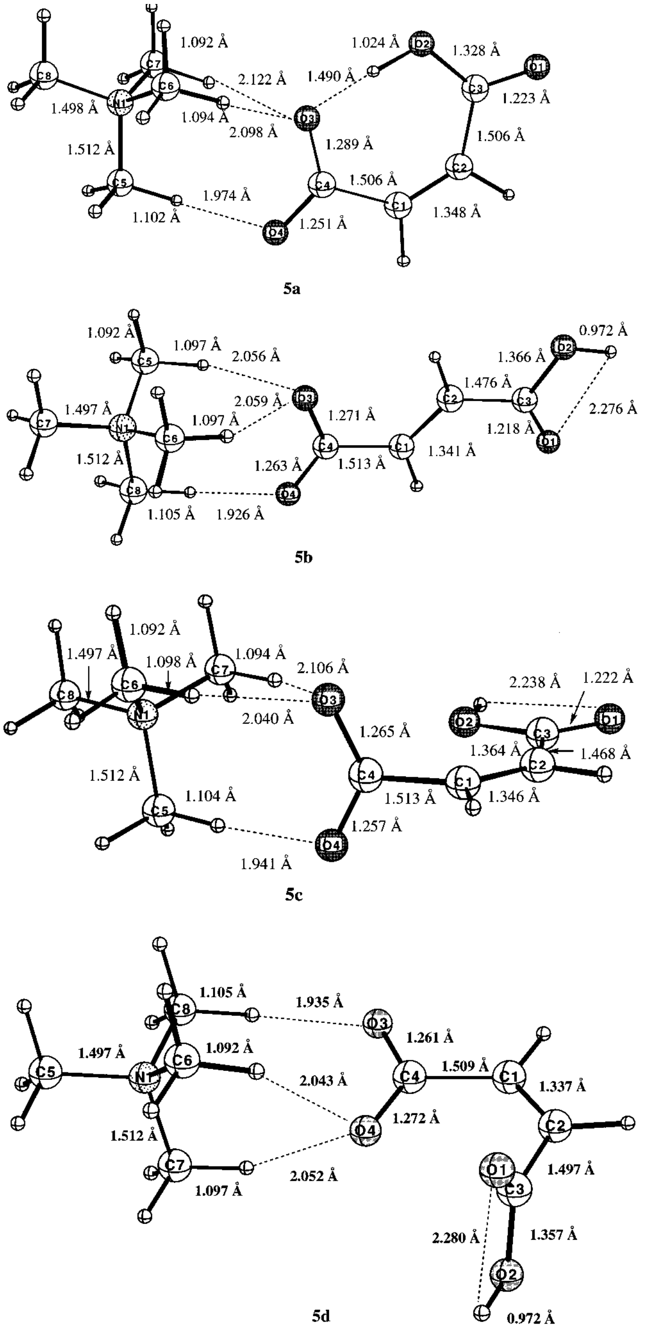

**Figure 5.** Optimized (B3LYP/6-31+G**) complexes between maleate anions and Me$_4$N$^+$ with (**5a**) and without (**5b** and **5c**) the internal hydrogen bond in the maleate molecule. Their relative energies are given in Table 3.

in maleate anion **1a** (O$\cdots$O are 2.415 and 2.442 Å at the B3LYP/6-31+G** and QCISD/6-31+G** levels, respectively).[19]

The fully optimized complexes of maleic and fumaric monoanions with Me$_4$N$^+$ (**5a** and **5b**, Figure 5) lead to a free energy difference of only $\Delta\Delta G$ = 4.3 kcal/mol in favor of the internally H-bonded *Z*-maleate complex **5a** (Table 3). When the free energy difference between maleic and fumaric acids is included (fumaric acid **1d** is 2.5 kcal/mol more stable than maleic, **1c**, Table 2), this estimate of the *relative* H-bond strength is 6.8 kcal/mol (based upon $\Delta\Delta G$) at the B3LYP/6-31+G** level. This value is close to the experimental estimation for the lower limit ($\Delta\Delta G$ = 5.5 kcal/mol) of the relative strength of the putative LBHB vs the normal H-bond in mesaconic acid in a nonpolar solvent.[4d] However, neither study has considered the effect of intermolecular H-bonding[2d] on this free energy difference. The difference in the external mode of H-bonding between Me$_4$N$^+$ and the *E*- and *Z*-maleate isomers indicates that the internal H-bond energy obtained above has to be supported by alternative estimations. Thus, if the complex of fumaric monoanion **3b** is used as the reference structure (**5c**), the estimate of the strength of the hydrogen bond in **5a** ($\Delta\Delta G$) is 9.3 kcal/mol ($\Delta E$ = 11.3 kcal/mol in methanol). The electrostatic stabilization of these maleate anions is also in evidence in the greatly attenuated energy differences between *Z*-maleate anion **1a** and naked anions **3b** (19.5 kcal/mol) and **3c** (23.4 kcal/mol, Table 1) relative to when they are complexed to tetramethylammonium ion as in **5c** and **5d** (1.2 kcal/mol, Table 3).

The calculated structure for Me$_4$N$^+\cdot$*Z*-maleate salt **5a** closely resembles that of its X-ray structure[20a] (X-ray **A**, Figure 6). The short intramolecular hydrogen bond between the carboxylic groups was clearly in evidence with an O$\cdots$O distance of 2.51 Å in **5a** and 2.4 Å in X-ray **A**. The carboxylate oxygen−nitrogen bond distances in **5a** are 3.47 (N$_1$−O$_3$) and 3.84 Å (N$_1$−O$_4$) while these corresponding bond distances in X-ray **A** are slightly

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(18) The geometry optimization of **1a** at the QCISD/6-31+G** level led to a shorter O−H bond length and a longer O$\cdots$H distance in **1a** (1.066 and 1.376 Å, respectively) than those optimized at the B3LYP/6-31+G** level (1.128 and 1.288 Å, respectively). The transition structure **3d** optimized at the QCISD/6-31+G** level has slightly shorter O$\cdots$H distances (1.194 Å) when compared with the B3LYP/6-31+G** values (1.201 Å).

(19) (a) These values in maleate anion agree with experimental estimates (2.40−2.44 Å)[19c] for some salts of maleic acid although the O$_3\cdots$O$_4$ distance in **1a** can change upon the complexation with a cation. (b) A value of $\leq$2.40 Å for the O$\cdots$O distance in O−H$\cdots$O hydrogen bonds has been suggested as a threshold for the formation of symmetrical O−H$\cdots$O hydrogen bonds.[19d] While the O$_3\cdots$O$_4$ distance in **1a** is rather close to this threshold, this distance becomes considerably larger in complex **5a** (2.511 Å). (c) Rios, M. A.; Rodriguez, J. *Can. J. Chem.* **1993**, *71*, 303. (d) Gilli, P.; Bertolasi, V.; Ferretti, V.; Gilli, G. *J. Am. Chem. Soc.* **1994**, *116*, 909.

(20) (a) Drobez, S.; Golic, L.; Leban, I. *Acta Crystallogr.* 1985, *C41*, 1503. (b) Jessen, S. M.; Kuppers, H. *J. Mol. Struct.* **1991**, *263*, 247. (c) A referee has questioned whether the carboxylate anion can actually hydrogen bond to the innermost CH$_2$ group of Bu$_4$N$^+$ or will the alkyl chains interfere. This prompted us to locate H-bonded complexes with both Et$_4$N$^+$ and Bu$_4$N$^+$ cations. Because of the size of these systems our geometry search was limited to the 6-31G* basis set. The similar geometries of the Me$_4$N$^+$ complexes with a larger basis set suggests that this is a reasonable approximation. (d) The H-bond strength of this SSHB in **8a** (O$_1$−O$_4$ = 2.546 Å) in the presence of an ammonium cation is in excess of 13 kcal/mol. Since both **8a** and **8c** have the *Z*-configuration of the double bond, this presents a more accurate measure of the actual H-bond strength in these complexes than the more traditional *E*/*Z* approach where the relative energies of the *E* versus the *Z* carbon−carbon double bonds comes into play.

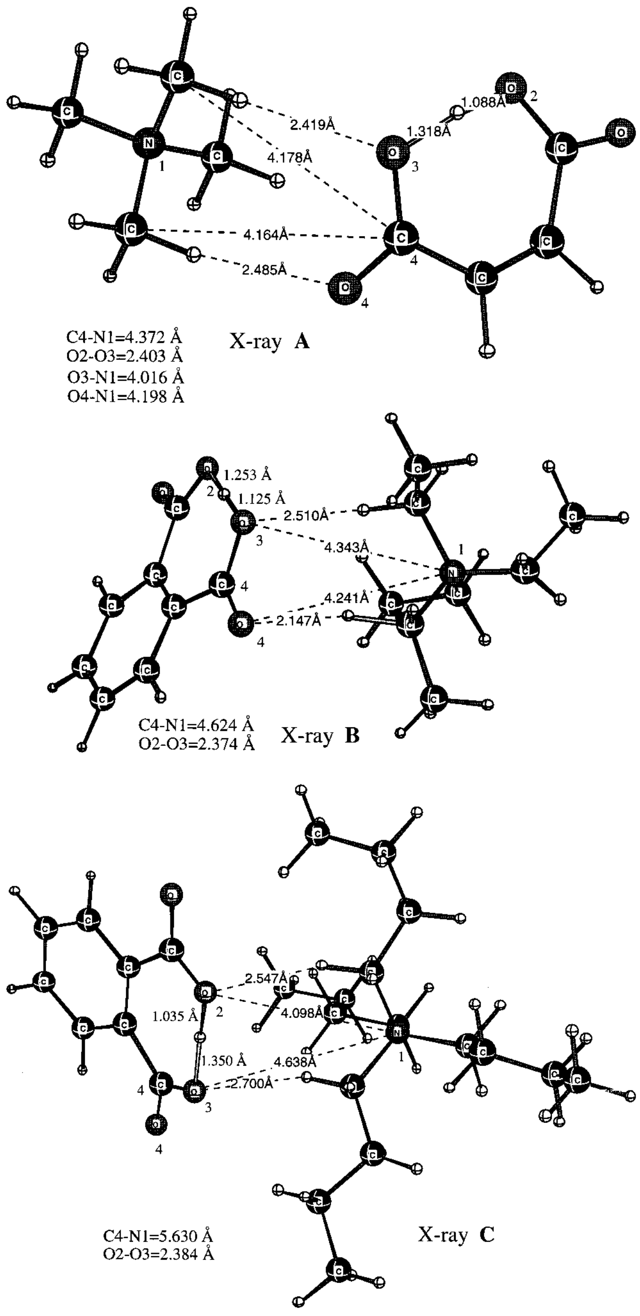


**Figure 6.** X-ray structures and selected geometrical characteristics representing interaction of *Z*-maleate with tetramethylammonium (**A**), tetraethylammonium (**B**), and tetrabutylammonium (**C**) cations.

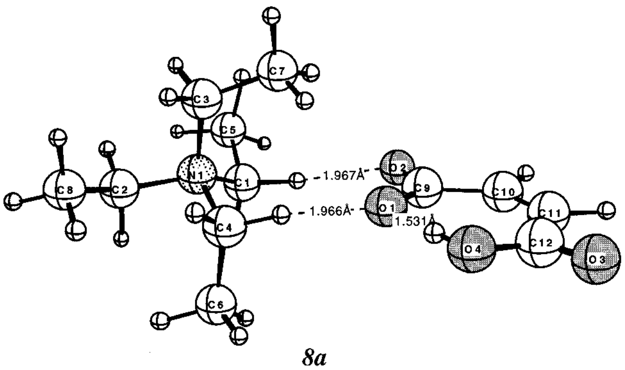
longer at 4.02 and 4.2 Å. *The hydrogen bonding interactions between the carboxylate oxygens and the methyl groups are clearly in evidence in both the theoretical and X-ray structures.* The C−H···O bond distances given in Figure 6 are estimated.

The calculated Mulliken charge on the nitrogen atom of the free $Me_4N^+$ cation itself is −0.23 while each of the four methyl groups has a compensating positive charge of 0.31. The net charge on the tetramethylammonium ion fragment in complex **5a** is +0.88 while the Mulliken charge on the nitrogen atom in $Me4N^+$ is even more negative (−0.59) in the complex (B3LYP/6-31+G** level). The distance between this *negatively* charged nitrogen and the positively charged (+0.49) carboxyl carbon atom is 4.08 Å in **5a** and 4.37 in X-ray **A**. Quantum calculations with a polarizable conductor model[15a] were used to provide an estimate of the hydrogen bond strength of these monoanions in the presence of a counteranion. When the dielectric constant approaches that of methanol there is a leveling effect and no further decrease in energy is observed.[6a] The dipole moment of **5b** ($\mu = 15.9$ D) is larger than that of **5a** ($\mu = 12.7$ D) and the COSMO solvent correction decreases the relative energy of **5b** with respect to **5a** from 5.1 kcal/mol in the gas phase to 4.4 kcal/mol in $CHCl_3$. In methanol, the energy difference between *E*- and *Z*-maleate monoanions is drastically reduced in both experiment[4d] and COSMO modeling, $\Delta\Delta E = 1.1$ kcal/mol (Table 3, the total energies from COSMO calculations on **5a** and **5b** are given in the Supporting Information, Table S1).

The reduction in H-bond strength in *neutral salt* **5a** appears to be principally a function of the charge neutralization in anion **1a** due to the presence of the tetraalkylammonium cation. As a further check on this idea we examined the energy differences between maleate anions **1a** and **1b** hydrogen bonded to *neutral* trimethylamine. The energy difference between the *anionic complexes* **6a** and **6b** (Figure S1, Supporting Information) of these *Z*- and *E*-maleate monoanions with $Me_3N$ is 13.4 kcal/mol at the B3LYP/6-31+G(d,p) level. This differs by only 1.2 kcal/mol from that of the naked anions themselves (**1a** and **1b**) and provides additional evidence of the impact of Coulombic effects on the strength of these intramolecular H-bonds. In other words, the H-bonding weakening due to the presence of the cation is due to the electrostatic interaction of opposite charges and not to the size of the system. Additional support for this idea follows from the fact that overall neutral complexes **7a** and **7b** (Figure 1S, Supporting Information) of anions **1a** and **1b** with $Me_3NH^+$ differ in energy by only 4.9 kcal/mol, a value very close to the 5.1 kcal/mol observed for the energy difference between neutral $Me_4N^+$ complexes **5a** and **5b**.

**Complexation with Tetraethylammonium Cation.** A systematic X-ray study[20b] of the effect of the different radii of the homologous series of tetraalkylammonium hydrogen phthalates on the effect upon inter- versus intramolecular hydrogen bonding provides an interesting insight into the principle question that we have raised: what is the effective distance between the *Z*-maleate carboxylate anion and the $Bu_4N^+$ cation? The tetramethyl, tetraethyl, tetrapropyl, and tetra-*n*-butyl salts of hydrogen phthalate did show a small increase in distance between the closest carboxylate oxygen and the "positive" nitrogen of the ammonium salt. The tetraethyl- and tetrabutylammonium salts both exhibited short intramolecular hydrogen bonds between the neighboring carboxylic oxygen with O···O distances of 2.374 and 2.385 Å (Figure 6), whereas the $Me4N^+$ salt has a slightly *larger* distance (2.403 Å) presumably because it is more tightly bound.

For the sake of comparison we located minima (B3LYP/6-31G*) for the complexation of *Z*- and *E*-maleate with tetraethylammonium cations, **8a** and **8b** (Figure 7).[20c] As anticipated, the *Z*-maleate anion is bound to the internal α-$CH_2$ group in complex **8a** and C−H···O distances of 1.97 Å suggest fairly strong external H-bonds consistent with an energy difference between these two complexes of 5.7 kcal/mol. The nearest oxygen-to-nitrogen distances in **8a** and X-ray **B** (Figure 6) are quite comparable (3.9 and 4.2 Å). The nitrogen−carboxylate carbon distance of 4.6 Å in X-ray **B** compares favorably with an N···$COO^-$ distance of 4.3 Å in **8a**. The nitrogen atom in $Et_4N^+$ bears a charge of −0.38 while each α-$CH_2$ group has a net charge of 0.25 which accounts for the rather strong Coulombic interaction between these two oppositely charged ions. The complexation energies of 88.4 and 99.0 kcal/mol for **8a** and **8b** (relative to isolated reactants) are somewhat less than

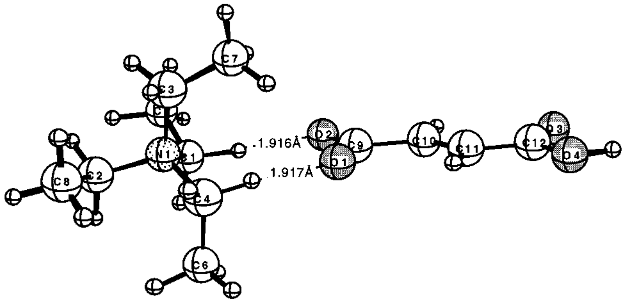


***8a***

$E_{tot.}$=-826.75427 a.u.

$E_{Rel}$= 0.0 kcal/mol

N1-O1=3.858 Å
N1-O2=3.909 Å
N1-C9=4.302 Å
C4-O1=3.057 Å
C1-O2=3.059 Å

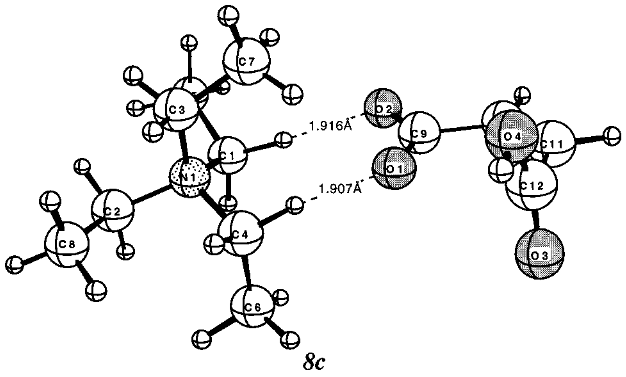


***8b***

$E_{tot.}$=-826.74523 a.u.

$E_{Rel}$= 5.7 kcal/mol

N1-O1=3.842 Å
N1-O2=3.839 Å
N1-C9=4.225 Å
C4-O1=3.016 Å
C1-O2=3.016 Å



***8c***

$E_{tot.}$=-826.73395 a.u.

$E_{Rel}$= 12.8 kcal/mol

N1-O1=3.823 Å
N1-O2=3.849 Å
N1-C9=4.222 Å
C4-O1=3.006 Å
C1-O2=3.016 Å

**Figure 7.** Optimized (B3LYP/6-31G*) complexes between maleate anions and $Et_4N^+$ with (**8a**) and without (**8b** and **8c**) internal hydrogen bond in the maleate molecule.

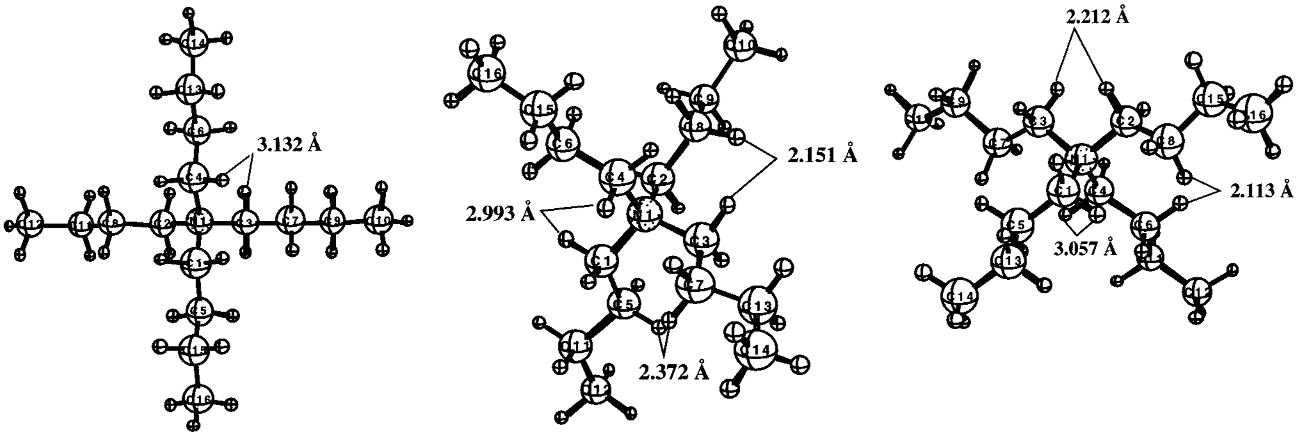
that noted above for **5a** and **5b** reflecting the increasing size and hence increasing stability of the gas-phase cation.

In the second approach, the O−H hydrogen in *Z*-maleate is rotated 180° around the C−O bond axis as in **3c** to “turn off” the H-bonding interaction. *Z*-Maleate complex **8c** is essentially anion **3c** hydrogen bonded to the tetraethylammonium cation. The difference in energy between **8a** and **8c** (12.75 kcal/mol) provides a measure of the *relative* strength of the internal H-bond to the carboxylate oxygen versus the neutral carbonyl oxygen of the carboxylic acid.[20d] Additionally, complex **8d** (Supporting Information, Figure S2), containing the anion of **3b** geometry, was optimized using the B3LYP/6-31+G (d,p) basis set and compared to **8a** re-optimized at the same level (**8a′**, Supporting Information, Figure S2). This estimate with the larger basis set suggests an H-bond strength of 11.4 kcal/mol, which agrees well with the above values.

**Complexation with Tetra-*n*-butylammonium Cation.** The question remains as to the validity of the use of smaller tetraalkylammonium ions as models for the much larger and perhaps more sterically demanding tetra-*n*-butylammonium ion.[20] First we resolved the question of the structure of $Bu4N^+$ itself and what influence its steric bulk might have on the approach of the maleate anions. A basic premise of the experimental studies of tetra-*n*-butylammonium salts of *E*- and *Z*-hydrogen maleates is that the four *n*-butyl groups would sterically shield the “positive” nitrogen of $n\text{-}Bu_4N^+$ sufficiently that the maleate anions would be essentially “naked anions”. Since the more electronegative nitrogen atom in such $R_4N^+$ cations is always *negative*, the four $-CH_2-$ groups α to the nitrogen, in fact, bear most of the net *positive* charge of +1 that resides on the tetraalkylammonium cation fragment.

We found at least three minima (analytical frequency at B3LYP/6-31G*) for $Bu4N^+$ with the T-shaped molecule of higher symmetry (**I**, Figure 8) being 0.8 kcal/mol lower in energy than the apparently more hindered ammonium cation **II** and 6.1 kcal/mol more stable than cation **III**. Although the rather flat surface of ammonium cation **I** would appear to present the best opportunity for complexation to the positively charged α-$CH_2$ groups, we chose the more hindered ammonium salt **II** to find complexes **9a** and **9b** (Figure 9) since this may better serve to resolve the controversy[20] concerning the steric inhibition to complexation. It also more closely resembles the $Bu_4N^+$ fragment in X-ray structure **C** (Figure 6). However, one should be aware of the noticeable difference in the mode of H-bonding in X-ray structure **C** with respect to **A** and **B** that is bound to the $Bu_4N^+$ by only one carboxylate group. Consequently, we optimized the geometry of the comparable salts, **9a*** and **9b*,** using a starting geometry based upon the X-ray coordinates of structure **C**. Both carboxylate moieties of the phenolate anion are H-bonded to the α-H−C of $Bu_4N^+$. Despite multiple intermolecular H-bonds to the *n*-butyl groups in **9a***, its energy is slightly higher (1.8 kcal/mol) than that of **9a**. The most important message of these two *Z*-maleate salts is that the phenolate anion (Figure 6) is still tightly bound to the $Bu_4N^+$ cation despite any potential steric hindrance. The charge on the nitrogen in $Bu_4N^+$ is also −0.38 but the *positive* charges on the α-, *β*-, and *χ*-$CH_2$ groups fall off rapidly as the distance from the electronegative nitrogen atom increases (0.224, 0.041, and 0.045, respectively).

The C−H···O bond distances of 2.02 and 2.04 Å and a distance of only 4.3 Å between the carboxylate carbon and the negatively charged nitrogen (−0.41) in **9a,** and the positively charged α-CH2 group (Figure 9) are consistent with a tight or intimate ion pair (the NBO charges on nitrogen and the α-CH2



**Cation I**

**$E_{rel}$ = 0.00**

**Cation II**

**$E_{rel}$ = 0.82**

**Cation III**

**$E_{rel}$ = 6.12**

**Figure 8.** Selected conformations of tetra-*n*-butylammonium cation optimized at the B3LYP/6-31G* level. The relative energies are given in kcal/mol.

groups are −0.28 and 0.26). The higher energy (14.6 kcal/mol) *E*-maleate anion is even more tightly bound to $Bu_4N^+$ with O···H−C hydrogen bonding distances of less than 2 Å. The binding energies relative to isolated reactants for formation of overall neutral salts **9a** and **9b** are 80.3 and 90.7 kcal/mol, respectively. The energy difference between complexes **9b** and **9a** is 5.8 kcal/mol. With an *E*/*Z* double bond correction of 2.5 kcal/mol, as above, the estimated H-bond strength is 8.3 kcal/mol.

In Table 4, we have summarized the estimates for the H-bonding energies in the maleate anions performed in this study. A comparison of the results presented indicates that the *E*/*Z* approach provides the lowest values for the internal H-bonding energy, whereas the use of a non-hydrogen bonding conformer, **3c**, as a reference structure gives somewhat higher estimates. Nevertheless, the weakening of the H-bonding interactions by 1.5−2 times due to the charge neutralizing complexation follows from these data.[21] It is also an important observation that *the size of the tetraalkylammonium salt does not affect the internal H-bond weakening,* which becomes clear by comparing **5a**, **8a**, and **9a**. In all three complexes the external bonding to the tetraalkylammonium cation involves hydrogens at the α-carbons. This provides a similar spacial arrangement of the interacting charged species, and, therefore, a comparable electrostatic effect.

Our observations should also have a major impact upon the interpretation of the NMR spectra of these ionic complexes. Proton transfer to the adjacent oxygen ($O_3$) in complex **5a** does not result in the formation of an energy minimum if the counterion is not allowed to move. When the $O_3$−H bond is constrained to 0.96 Å an increase in energy of 15 kcal/mol is observed. Release of this bonding constraint results in rapid reversion to **5a**. Similarly, inclusion of two water molecules to complex with the carboxylate end of **1a** to simulate such asymmetric solvation in an aqueous environment leads to a highly unsymmetrical H-bond. When the hydrogen was transferred to acceptor oxygen ($O_3$) we again observed that a minimum does not exist. When the $O_3$−H bond was constrained to 0.96 Å the energy was increased by 8.3 kcal/mol, respectively. Release of the O−H bond constraint afforded the original complex **1a** hydrogen bonded to the two water molecules. The SCRF method applied to the tetrahydrate of both closed and open forms of hydrogen maleate gave a free energy difference of −0.73 kcal/mol slightly favoring the open form.[22a] The influence of solvent on the proton transfer reaction has also been extensively studied by molecular-dynamic simulation.[22b]

In a nonpolar solvent the barrier for proton transfer within an intimate ion pair should increase markedly when the intramolecularly hydrogen bonded anion is electronically asymmetric. Indeed, crystals found with asymmetric H-bonds have asymmetrically placed counterions.[5b] These data suggest that an enzyme would also be required to have a highly symmetrical electronic environment for a SSHB to function as suggested. Although the rate for proton transfer in an electronically symmetrical environment (e. g. naked anion **1a**) is essentially barrierless, even a diffusion-controlled migration of the counterion will have difficulty maintaining electronic neutrality. Therefore, the experimental estimates based on Scheme 1, which gives the relative strength of the hydrogen bond as a salt of maleate anion and $Bu_4N^+$ with respect to that in maleic acid, are significantly impacted by the presence of $Bu_4N^+$. It has generally been assumed in the NMR experiments that the bulky $Bu_4N^+$ counterion used in organic solvents does not associate closely with the carboxylate groups.

**Hydrogen Bonding in Bifluoride.** Traditional H-bonds are considered to vary from 3 to 7 kcal/mol. However, exceptionally strong hydrogen bonding in bifluoride anion has been taken as prima facea evidence for the existence of short-strong hydrogen bonds. While the H-bond between HF and $F^-$ has a reported value of −46 kcal/mol in the gas phase, it is only −0.82 kcal/mol in aqueous solution. The above data on the intramolecular

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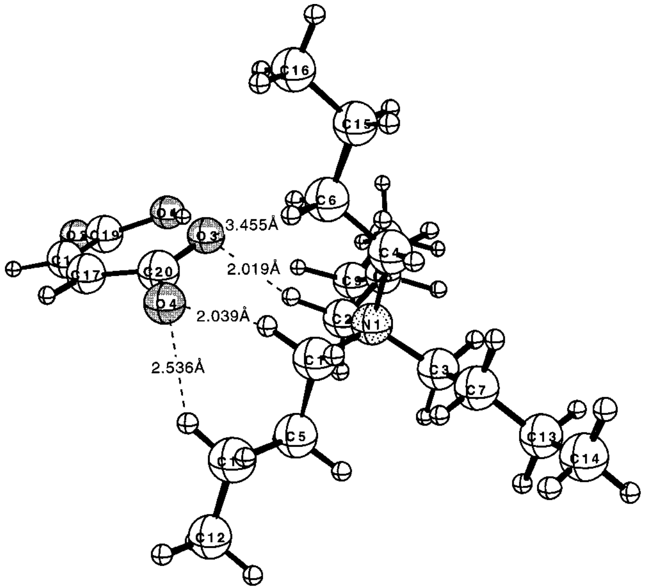
[21] Natural Bond Orbital (NBO) analyses (Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.) implemented in Gaussian 98 have been performed on *E*- and *Z*-maleate (**1a**,**1b**) and *Z*-maleate complexed to $Me_4N^+$ (**5a**) and $Bu_4N^+$ (**9a**) following B3LYP/6-31+G(d,p) optimization. We have examined all estimates of bonding−antibonding orbital interactions between "filled" and "empty" NBOs and found that in *Z*-maleate **1a** the OH-antibonding orbital (electron acceptor) and oxygen lone pair (electron donor) is a major interaction. Thus, the electron occupancy of the OH-antibonding orbital can be considered as a measure of this stabilizing interaction and, consequently, a measure of the H-bond strength. In naked *E*-maleate (**1b**), the electron occupancy is quite low (0.016), in *Z*-maleate (**1a**) it is 0.195, and in **5a** and **9a** it is about 1.8 times smaller (0.110 and 0.106). This number is in excellent agreement with the 1.5−2 estimate based upon energetic changes.

[22] (a) Marvi, J.; Hadzi, D. *J. Mol. Struct. (Theochem)* **1998**, *432*, 257. (b) Marvi, J.; Berendsen, H. J. C.; Vangunsteren, W. F. *J. Phys. Chem.* **1993**, *97*, 13469.

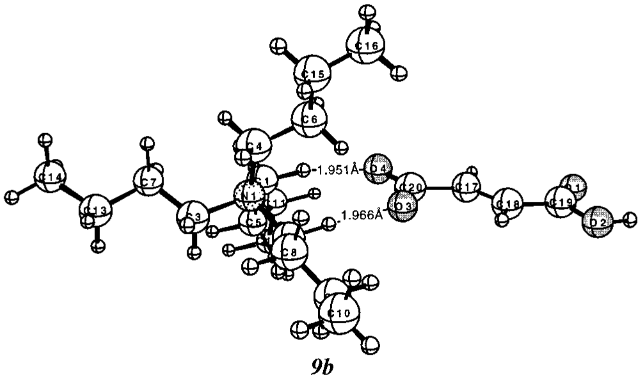


*9a*

$E_{tot.}$=-1141.26654 a.u.

$E_{Rel}$= 0.0 kcal/mol

N1-O3=3.919 Å
N1-O4=3.922 Å
N1-C20=4.307 Å
C1-O4=3.081 Å
C2-O3=3.084 Å

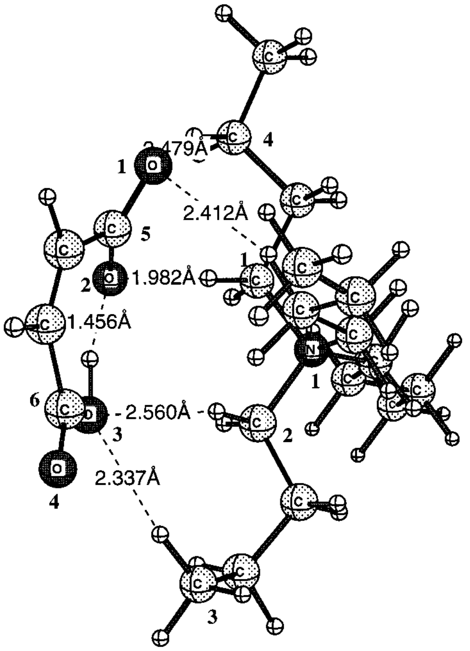


*9b*

$E_{tot.}$=-1141.25735 a.u.

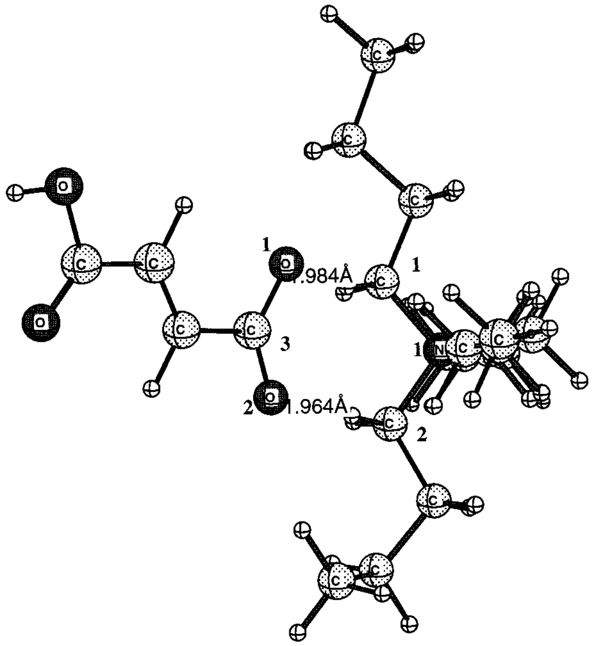
$E_{Rel}$= 5.8 kcal/mol

N1-O3=3.910 Å
N1-O4=3.838 Å
N1-C20=4.262 Å
C1-O4=3.026 Å
C2-O3=3.034 Å



*9a**
$E_{tot.}$=-1141.26368 a.u.
$E_{Rel}$= 0.0 kcal/mol

N1-O1=4.735 Å; N1-C5=4.571 Å
N1-O2=3.861 Å; N1-C6=5.553 Å
N1-O3=4.528 Å; O2-O3=2.479 Å
C1-O2=3.074 Å; C3-O3=3.425Å
C2-O3=3.615 Å; C4-O1=3.502Å



*9b**

$E_{tot.}$=-1141.25766 a.u.

$E_{Rel}$= 3.8 kcal/mol

N1-O1=3.941 Å
N1-O2=3.799 Å
N1-C3=4.262 Å
C1-O1=3.060 Å
C2-O3=3.058 Å

**Figure 9.** Structures and selected geometrical characteristics for the complexes between maleate anions and $Bu_4N^+$ optimized at the B3LYP/6-31G* level. Their relative energies are discussed in the text.

hydrogen bonding interactions in *Z*-maleate in the presence and absence of a counterion clearly implicate electrostatic stabilization by the ammonium cation as the discerning factor in reducing the hydrogen bond strength in these model diacid monoanions. This prompted us to examine also the effect of a sodium cation on the H-bond strength of the paradigm strong hydrogen bond

**Table 4.** Relative Energies (B3LYP/6-31+G(d,p)) of Various Configurations of Maleate Anion Itself and Complexed with Tetraalkylammonium Cations[a]

| structures | maleate anion | maleate anion + $Me_4N^+$ | maleate anion + $Et_4N^+$ | maleate anion + $Bu_4N^+$ |
|---|---|---|---|---|
| *Z*-maleate anion **1a**, **5a**, **8a**, **9a** | 0 | 0 | 0 | 0 |
| *E*-maleate anion **1b**, **5b**, **8b**, **9b** | 14.6 (15.7)[b] | 5.1 (4.9)[b] | 5.7[c] | 5.8[c] |
| *Z*-maleate anion (planar)[d] **3a**, | 26.7 (27.9)[b] | | | |
| *Z*-maleate anion **3b**, **5c**, **8d**[e] (COO is twisted) | 19.5 (20.6)[b] | 10.7 (10.2)[b] | 11.4 | |
| *Z*-maleate anion ($CO_2H$ is twisted) **3c**, **5d**, **8c** | 23.4 (24.4)[b] | 11.9 (11.4)[b] | 12.8[c] | |

[a] The numbers obtained by the *E*/*Z* approach have to be corrected for Δ*E*(cis−trans) (2.5−3.6 kcal/mol, Table 2) to be compared with H-bonding energy estimations. [b] Δ*E*+ ZPE(B3LYP/6-31+G**) values are given in parentheses. [c] At the B3LYP/6-31G(d) level. [d] A second-order saddle point, hydrogen atom is rotated away in order to exclude H-bonding. [e] Structure is given in Supplemental Information, Figure S2; dihedral angle O(H)CCC in the noninteracting maleate part was constrained to 0° in order to preserve planarity and absence of any additional H-bonding introductions.

**Table 5.** Complexation Energies[a] of Various Complexes[b] of NaF and HF

| complexes | Δ*E* B3LYP/ 6-31+G** | Δ*E* SCIPCM// B3LYP/6-31+G** |
|---|---|---|
| HF + HF → HF···HF | −5.1 | −8.8 |
| HF + NaF → HF···NaF | −31.9 | −36.4 |
| HF + $F^-$ → HF···$F^-$ | −47.4 | −59.3 |
| NaF + $F^-$ → NaF···$F^-$ | −62.5 | −60.2 |
| NaF + NaF → NaF···NaF | −58.4 | −40.4 |

[a] In kcal/mol.

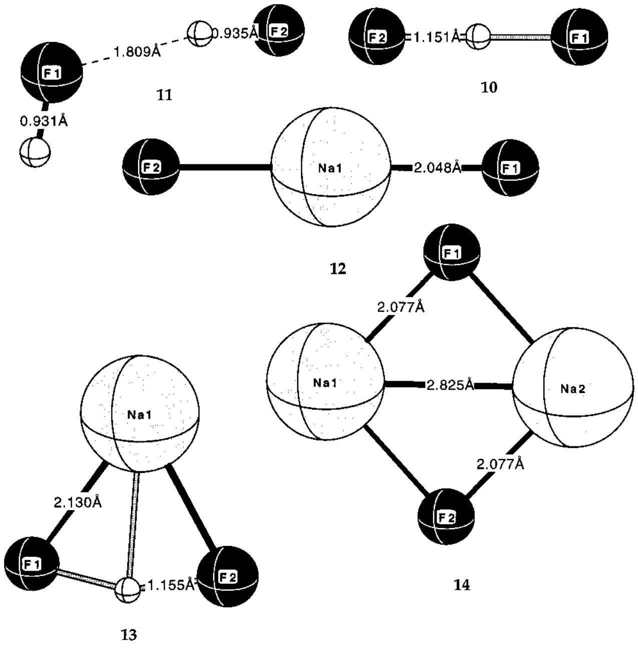


**Figure 10.** HF and NaF complexes **10**−**14** optimized at the B3LYP/6-31+G** level and their selected geometrical characteristics.

in gas-phase bifluoride $FHF^-$ **10** (Figure 10). While the dimerization energy of HF is −5.1 kcal/mol (a normal H-bond, **11**) the H-bond strength in the H···F−$H^-$ anionic complex is, as anticipated,[23] −47.4 kcal/mol (B3LYP/6-31+G**). When a sodium cation is included the stabilization energy of neutral complex **13**, NaF···HF, is reduced to −31.9 kcal/mol (Table 4) but this value is still surprisingly high relative to the magnitude of the H-bond in the maleate anion complexed to an ammonium cation. However, this interaction is largely electrostatic in nature as evidenced by the complexation energy of sodium fluoride with a fluoride anion **12** (−62.5 kcal/mol) and the stabilization energy accompanying the dimerization of NaF **14** (−58.4 kcal/mol, Figure 10). These interaction energies, *in the total absence of a hydrogen bond*, are thus *larger* than the celebrated bifluoride $F^-$···HF binding energy. The marked effect of aqueous solution on the H-bonding energies of the $F^-$···HF complex (0.8 kcal/mol) prompted us to also examine the binding energies of these complexes using the SCIPCM model ($\epsilon = 78$). The stabilization energies for those complexes bearing hydrogens are modestly *increased* by the simulated aqueous environment (where H-bonding interactions are not treated explicitly) but are somewhat reduced for the complexes where only sodium ions are involved. Thus, solvent separated ion pairs in aqueous solution will be expected to exhibit only minimal H-bonding strengths while an intimate ion pair such as we have above for ammonium complex **5a** in a nonpolar solvent will exhibit an intermediate H-bonding interaction compared to that of a gas-phase anion.

## 4. Summary

We have thus resolved the apparent controversy between experiment and theory and shown that while strong ionic hydrogen bonds can exist in anions in the gas phase, whether they can also be strong in a condensed media depends on how their interactions with the environment affect their strength. The present controversy is centered around the discrepancy between gas-phase calculations on naked anions and experimental data garnered in solution in the presence of a counterion. Our data clearly indicate that such gas-phase calculations are in excellent agreement with experiment provided the electrostatic effects of a counterion are explicitly treated in the calculation. The calculated energy difference between *E*- and *Z*-maleate complexed to $Me_4N^+$, $Et_4N^+$, and $Bu_4N^+$ cations are 5.1 (B3LYP/6-31+G(d,p)) and 5.7 and 5.8 kcal/mol (B3LYP/6-31G(d)). ZPE correction for the $Me_4N^+$ salt results in somewhat smaller value, 4.9 kcal/mol. Simply stated, it is not the dielectric environment that is in question but the charge neutrality that seems to be at the root of this controversy.

The computational estimates for the intrinsic strength of the hydrogen bond in the gas-phase naked maleate anion, which are in a range of 14−28 kcal/mol depending on the choice of the reference structure, should not be directly compared with the experimental data for condensed media. The estimated range (8−13 kcal/mol) for the internal H-bonding interaction in tetraalkylammonium/maleate complexes is 1.5−2 times smaller than in the naked anion and is largely independent of the overall size of the cation. More importantly, these data suggest that site-specific electrostatic interactions can also potentially influence the energetics of H-bond dependent enzymatic processes involving charge alteration along the reaction pathway. We conclude from these data that the estimated intramolecular hydrogen bonding in these monoanion−ammonium cation complexes is relatively small based upon the *E*/*Z* approach as suggested by experiment. However, the magnitude of this ionic

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[23] (a) Wenthold, P.; Squires, R. *J. Phys. Chem.* **1995**, *99*, 2002. (b) Kresge, A. J.; Chaing, Y. *J. Chem. Phys.* **1973**, *77*, 822. (c) Larson, J. W.; McMahon, T. B. *J. Am. Chem. Soc.* **1982**, *104*, 6255.

interaction can be in excess of 13 kcal/mol when based upon the $Et^4N^+$ cation hydrogen bonding to the non-hydrogen bonding conformer of *Z*-maleate anion **3c**.

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**Supporting Information Available:** Table S1 (total energies of structures **1a**,**b**, **3a**,**b**,**c**,**d**, and **5a**,**b** in gas phase, and in solvent), Figure S1 (selected geometrical parameters of complexes between maleate anions and $Me_3N$ (**6a**, **6b**) and $Me_3NH^+$ (**7a**, **7b**) cation optimized at the B3LYP/6-31+G** level), and Figure S2 (*Z*-maleate/$Et_4N^+$ complexes **8a** and **8d** optimized at the B3LYP/6-31+G(d,p) level for an additional estimation on H-bonding energy in *Z*-maleate) (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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