5152 J. Am. Chem. Soc. 1989, 111, 5152-5155

A Theoretical Study of the Change in Homolytic Bond Dissociation Energy on Conversion of A–B to A–B$^+$H

Russell J. Boyd,* J. N. Mark Glover, and James A. Pincock*

Contribution from the Department of Chemistry, Dalhousie University, Halifax, Nova Scotia B3H 4J3, Canada. Received August 16, 1988

Abstract: The bond dissociation energies (BDE) for the homolytic cleavage of a number of isoelectronic A–B dimers have been calculated to third order in Møller–Plesset perturbation theory with the 6-31G** basis set. In particular, BDE's have been calculated for A–B → A$^\bullet$ + $^\bullet$B, with A = CH_3, NH_2, OH, and F and B = CH_3, NH_2, OH, F, N^+H_3, O^+H_2, and F^+H. It is shown that a substantial increase in the BDE occurs upon protonation of A–B and that the more electronegative the element B, the greater the change in BDE that accompanies the protonation of B. It is also observed that the greater the electronegativity difference between A and B, the greater the change in BDE due to protonation and that the change in BDE that accompanies protonation of homoatomic molecules decreases with increasing atomic number. These trends are rationalized by application of the earlier discussions of Pauling and Allred and shown to be consistent with known chemical transformations.

The strength of a chemical bond is of fundamental importance in any consideration of chemical reactivity. As an example, there has been considerable interest in the process of excited-state bond cleavage that occurs on irradiation of substrates containing a benzylic carbon attached to a leaving group. The products can be rationalized in terms of either the arylmethyl cation resulting from heterolytic cleavage or the arylmethyl radical resulting from homolytic cleavage (eq 1). The subject has been extensively

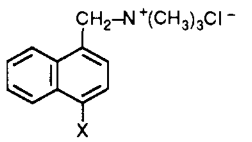
$$ArCH_2X \xrightarrow{h\nu} ArCH_2{}^+X^- \text{ or } ArCH_2{}^\bullet\ {}^\bullet X \qquad (1)$$

reviewed.[1] The competition between these two possible pathways depends on many factors including the nature of the aryl group, the nature of the leaving group, and the multiplicity (singlet vs triplet) of the excited state in ways which are not yet well understood.

Clearly, another critical factor in these bond cleavage processes is the C–X bond strength. This is true even for excited-state processes because, unless the excitation energy is greater than the bond strength, efficient bond fragmentation is impossible. Good estimates of bond dissociation energies can be obtained from thermochemical data when X is neutral. However, many of the leaving groups that undergo efficient photochemical cleavage are positively charged (C–N^+R_3,[2,3] C–O^+H_2,[4,5] C–S^+R_2,[2,6,7] and C–P^+R_3[7]), and no bond strength information is available. At first sight, the heterolytic cleavage pathway (eq 2) to form the arylmethyl cation and the neutral X may appear to be more favorable,

$$ArCH_2\text{–}X^+ \xrightarrow{h\nu} ArCH_2{}^+X \text{ or } ArCH_2{}^\bullet\ X^{\bullet +} \qquad (2)$$

particularly in polar solvents. This is certainly true for the corresponding ground-state solvolysis chemistry. However, examples of excited-state homolytic cleavage to the arylmethyl radical and a radical-cation fragment are common. For example, the ratio of products obtained from the excited singlet state in methanol by heterolytic versus homolytic intermediates is 3:1 for **1**[2] and 1:2 for **2**.[3] The triplet states of both are unreactive.



1, X = H
2, X = CN

Table I. A–B Bond Dissociation Energies (kJ mol^{-1})[a]

fragment B	fragment A CH$_3$	NH$_2$	OH	F
CH_3	400 (406)			
NH_2	363 (389)	272 (305)		
OH	381 (410)	253	180 (230)	
F	439 (477)	259	158 (226)	102 (159)
N^+H_3	491 (476)	364 (357)	290	244
O^+H_2	555 (557)	377	265	140
F^+H	718 (1016)	518	327	137

[a] Experimental values in parentheses are from Hehre et al. (p 278)[11] for the neutral species or by the calculation outlined in eq 4 for the charged species.

In order to obtain some understanding of how a bond strength of a neutral molecule is altered by converting an atom with a lone pair of electrons into a positively charged atom, we have carried out ab initio molecular orbital calculations on simple model systems. In particular, we have calculated bond dissociation energies (BDE) for

$$A\text{–}B \rightarrow A^\bullet + {}^\bullet B \qquad (3)$$

with A = CH_3, NH_2, OH, and F and B = CH_3, NH_2, OH, F, N^+H_3, O^+H_2, and F^+H.

Computational Details

The calculated BDE's for the homolytic cleavage of 22 isoelectronic A–B dimers are listed in Table I. In each case the energies have been calculated to third order in Møller–Plesset perturbation theory[8] by use of the 6-31G** basis set[9] at the Hartree–Fock 6-31G*-optimized geometries.[10] Thus, the level of theoretical treatment is denoted[11] by MP3/6-31G**//HF/6-31G* but referred to herein as simply MP3/6-31G**. All calculations were performed with the GAUSSIAN 80 package[12] of programs. Three of the protonated species have been studied previously at the MP3/6-31G** level.[13]

The computed BDE's correspond to equilibrium values, D_e, whereas experimental values include the zero-point vibrational energy (ZPE) and are denoted by D_0. A direct comparison requires, therefore, subtraction of the ZPE from the theoretical D_e or addition to the experimental D_0. The experimental values in Table I include the ZPE correction.

---

(1) Cristol, S. J.; Bindel, T. H. *Organic Photochemistry*; Marcel Dekker: New York, 1983; Vol. 6, p 327.

(2) Arnold, B.; Donald, L.; Jurgens, A.; Pincock, J. A. *Can. J. Chem.* **1985**, *63*, 3140.

(3) Foster, B.; Gaillard, B.; Mathur, N.; Pincock, A. L.; Pincock, J. A.; Sehmbey, C. *Can. J. Chem.* **1987**, *65*, 1599.

(4) Wan, P. *J. Org. Chem.* **1985**, *50*, 2583.

(5) Turro, N. J.; Wan, P. *J. Photochem.* **1985**, *28*, 93.

(6) Maycock, A. L.; Berchtold, G. A. *J. Org. Chem.* **1970**, *35*, 2532.

(7) Breslin, D. T.; Saeva, F. *J. Org. Chem.* **1988**, *53*, 713.

(8) Pople, J. A.; Binkley, J. S.; Seeger, R. *Int. J. Quantum Chem. Symp.* **1976**, *10*, 1.

(9) This is a split-valence basis set with polarization functions on all atoms. Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.

(10) Whiteside, R. A.; Frisch, M. J.; Pople, J. A. *The Carnegie-Mellon Quantum Chemistry Archive*, 3rd ed.; Department of Chemistry, Carnegie-Mellon University: Pittsburgh, PA, 1983.

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

(12) Binkley, J. S.; Whiteside, R. A.; Krishnan, R.; Seeger, R.; DeFrees, D. J.; Schlegel, H. B.; Topiol, S.; Kahn, L. R.; Pople, J. A. Department of Chemistry, Carnegie-Mellon University, Pittsburgh, PA 15213.

(13) Nobes, R. H.; Radom, L. *Chem. Phys.* **1983**, *74*, 163.

0002-7863/89/1511-5152$01.50/0

Table II. Changes, $\delta\Delta$, in A–B Bond Dissociation Energies (kJ mol^{-1}) Due to Protonation of B

fragment B^+–H	fragment A					
	CH_3	NH_2	OH	F	$\delta\chi_{BH^+}$[b]	χ_{BH^+}[c]
N^+H_3	128	92	37	−15	0.54	3.58
O^+H_2	174	124	85	−18	0.69	4.13
F^+H	279	259	169	35	0.92 (1.24)[d]	4.90 (5.22)[d]
χ_A[a]	2.55	3.04	3.44	3.98		

[a] Electronegativity values are from Allred.[20] [b] Evaluated from the slopes of the plots in Figure 1. [c] By definition $\chi_{BH^+} = \delta\chi_{BH^+} + \chi_B$. [d] Omitting the point for CH_3–F^+H.

Hehre et al.[11] have shown that the MP3/6-31G** calculations lead to very similar results as fourth-order Møller–Plesset perturbation theory and that any residual errors (typically 20–40 kJ mol^{-1}) are due largely to the limitation of the 6-31G** basis set and not to truncation of the perturbation series expansion. Moreover, unpublished calculations by Pople[11] indicate that the MP3/6-31G** method should predict accurately the trends of interest in this paper.

Results and Discussion

Comparison of the theoretical BDE's with the experimental BDE's of eight neutral molecules (Table I) shows that in every case the theoretical value is less than the experimental value, but the major trends are reproduced. The direction of the error is readily understood in terms of correlation effects. Since homolytic cleavage requires the separation of an electron pair, the correlation energy is greater in the parent molecule than in the fragments, and since only a fraction of the correlation energy is recovered by the MP3 method, the calculated BDE's should be less than the experimental values. Higher order MP calculations would raise the theoretical BDE's.[11] Also, the correlation effects tend to be greater with small electronegative atoms, and thus the accuracy of our results is lower in F_2, for example, than in C_2H_6.[14]

Values of the experimental BDE for a few of the charged species can also be estimated by the thermodynamic relationship outlined in eq 4 and recently summarized by Pearson.[15] In essence the required quantities are the heats of formation of A–B$^+$H, A$^\bullet$, and B$^{\bullet+}$H. Experimentally, these can be obtained as follows: for A–B$^+$H from the heat of formation and the proton affinity (PA) of A–B; for A$^\bullet$ from thermochemical studies of reactions that generate the radical; for B$^{\bullet+}$H from the heat of formation and ionization potential (IP) of BH. In those cases where these values are available,[16,17] the derived BDE's are entered in Table I.

$$\text{A–B} \xrightarrow{\text{PA}} \text{A–B}^+\text{H} \xrightarrow{\text{BDE}} \text{A}^\bullet\ \text{B}^{\bullet+}\text{H} \xleftarrow{\text{IP}} \text{BH} \qquad (4)$$

The results in Table I reveal that the calculated values for the neutral A–B species show two trends that agree with experimental values: (i) the BDE decreases monotonically along the series CH_3–CH_3, NH_2–NH_2, HO–OH, F–F; and (ii) the BDE passes through a minimum at CH_3–NH_2 in the series CH_3–CH_3, CH_3–NH_2, CH_3–OH, CH_3–F.

Perhaps more revealing from our point of view are the results in Table II, which show the changes ($\delta\Delta$) in BDE that occur upon protonation of A–B; i.e., $\delta\Delta$ = BDE(A–B$^+$H) − BDE(A–B).[18] In general, these are large positive numbers, indicating that the bond strength is increased by protonation of B. The experimental values show the same effect although the relatively few values available make a complete analysis impossible. However, for the calculated values, some trends are obvious: (i) the more electronegative the element B, the greater the change in BDE that accompanies protonation; i.e., $\delta\Delta$ increases along the series CH_3–NH_2/CH_3–N^+H_3, CH_3–OH/CH_3–O^+H_2, CH_3–F/CH_3–F^+H; (ii) as the electronegativity difference between A and B increases, the change in BDE that accompanies protonation increases; i.e., $\delta\Delta$ increases along the series F–F/F–F$^+$H, HO–F/HO–F$^+$H, NH_2–F/NH_2–F$^+$H; (iii) the change in BDE that accompanies protonation of the homoatomic molecules decreases with increasing atomic number; i.e., $\delta\Delta$ decreases along the series NH_2–NH_2/NH_2–N^+H_3, HO–OH/HO–O^+H_2, F–F/F–F$^+$H.

The diprotonated species N^+H_3–N^+H_3, H_2O^+–O^+H_2, and HF^+–F^+H have not been included in Table I because they are unstable at the MP3/6-31G** level with respect to the fragments and thus lead to negative BDE's: −209, −419, and −618 kJ mol^{-1}, respectively. Nevertheless, local minima corresponding to the dimeric species were found on the respective potential energy surfaces with heavy-atom equilibrium bond lengths of 1.441, 1.368, and 1.376 Å, respectively.

From Pauling's original definition[19] of electronegativity as "the power of an atom in a molecule to attract electrons to itself", it is apparent that protonation of an atom will increase its electronegativity. In fact, one might expect that the changes in BDE's can be rationalized in terms of Pauling's original ideas[19] about the connection between the bond energy and the electronegativity difference between two bonded atoms. For instance, the calculated BDE of CH_3–NH_2, 363 kJ mol^{-1}, changes to 491 kJ mol^{-1} in CH_3–N^+H_3 because N^+H_3 is more electronegative than NH_2. Even the cases in Table II for which the changes in BDE are negative seem reasonable. If F–NH_2 is protonated on the less electronegative atom, nitrogen, to give F–N^+H_3, the increase in the electronegativity of that nitrogen will lead to a decrease in the electronegativity difference of the bonded atoms and hence a bond weakening.

These trends can be rationalized more quantitatively as follows. As stated by Allred,[20] "Pauling pointed out that the energy, E(A–B), of bonds between unlike atoms is usually greater than the average of the energies, E(A–A) and E(B–B), of the homoatomic bonds and that the extra ionic resonance energy, Δ(A–B), of the heteroatomic bond is related to the difference between the electron-attracting abilities of A and B". Equations 5 and 6 summarize this statement where the χ's are the appropriate electronegativities.[21,22]

$$\Delta(\text{A–B}) = E(\text{A–B}) - \frac{E(\text{A–A}) + E(\text{B–B})}{2} \qquad (5)$$

$$|\chi_B - \chi_A| = 0.102\{\Delta(\text{A–B})\}^{1/2} \qquad (6)$$

In order to consider the changes that occur on protonation of A–B, two similar equations can be written for A–B$^+$H:

$$\Delta(\text{A–B}^+\text{H}) = E(\text{A–B}^+\text{H}) - \frac{E(\text{A–A}) + E(\text{B–B})}{2} \qquad (7)$$

$$|\chi_{BH^+} - \chi_A| = 0.102\{\Delta(\text{A–B}^+\text{H})\}^{1/2} \qquad (8)$$

Subtracting eq 5 from eq 7 gives $\delta\Delta$ (eq 9), which defines the values listed in Table II.

$$\delta\Delta = \Delta(\text{A–B}^+\text{H}) - \Delta(\text{A–B}) = E(\text{A–B}^+\text{H}) - E(\text{A–B}) \qquad (9)$$

---

[14] In fact Hartree–Fock theory predicts F_2 to be unstable with respect to separated fluorine atoms: the HF/6-31G* value for the BDE is −137 kJ mol^{-1}.

[15] Pearson, R. G. *J. Org. Chem.* **1987**, *52*, 2131.

[16] Wagman, D. D. *J. Phys. Chem. Ref. Data* **1982**, *11* (No. 2).

[17] Lias, S. G.; Liebman, J. F.; Levin, R. D. *J. Phys. Chem. Ref. Data* **1984**, *13*, 695.

[18] The differences in BDE's may be more accurate than the BDE's themselves due to partial cancellation of correlation energies.

[19] Pauling, L. *The Nature of the Chemical Bond*, 3rd ed.; Cornell University Press: Ithaca, NY, 1960; Chapter 3.

[20] Allred, A. L. *J. Inorg. Nucl. Chem.* **1961**, *17*, 215.

[21] The value of the constant has been changed from Allred's value of 0.208 to 0.102 because the energies are in kilojoules per mole.

[22] Pauling[23] has argued that the so-called geometric mean, that is, $[E(\text{A–A})E(\text{B–B})]^{1/2}$, may be better in eq 5. For our treatment, there is no difference since the term disappears by subtraction.

[23] Reference 19; p 82.

Table III. Changes, δr, in A–B Bond Lengths (Å) Due to Protonation[a,b]

fragment B	fragment A: CH_3: HF	CH_3: MP2	NH_2: HF	OH: HF	F: HF
N^+H_3	0.054 (1.453)	0.045 (1.465)	0.015 (1.413)	−0.030 (1.403)	−0.053 (1.386)
O^+H_2	0.111 (1.400)	0.094 (1.424)	0.087 (1.403)	0.014 (1.397)	−0.022 (1.376)
F^+H	0.317 (1.365)	0.210 (1.392)	0.237 (1.386)	0.128 (1.376)	0.043 (1.345)

[a] All values except those in the column labeled MP2 are based on geometries optimized at the HF/6-31G* level. The data for CH_3F and CH_3F^+H are from ref 13. [b] The equilibrium bond lengths of the neutral species are shown in parentheses.

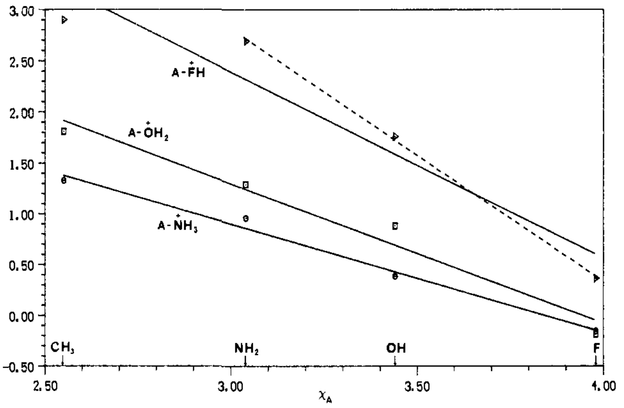


Figure 1. Graph of the change in bond energy due to protonation versus Allred's revised values of the Pauling electronegativities. The dashed line for the series $A–F^+H$ corresponds to omitting $CH_3–F^+H$ from the linear regression.

Taking the difference between the squares of eq 6 and 8 yields $\delta\Delta$ in terms of electronegativities.

$$(1.04 \times 10^{-2})\delta\Delta = (\chi_{BH}{}^2 - \chi_B{}^2) - 2\chi_A(\chi_{BH}{}^+ - \chi_B) \quad (10)$$

According to eq 10, the change in bond energy that results from converting A–B to $A–B^+H$ should be linear in the electronegativity of A with a slope equal to twice the change in electronegativity[24] due to protonation of B. Tests of this equation are shown in Figure 1 for the series $A–N^+H_3$, $A–O^+H_2$, and $A–F^+H$, where A = CH_3, NH_2, OH, and F.

The plots for the series $A–N^+H_3$ and $A–O^+H_2$ are reasonably linear (R^2 = 0.989 and 0.968, respectively) and give electronegativities of 3.58 and 4.14 for N^+H_3 and O^+H_2, respectively. It is the changes from the values for the corresponding neutral fragments, χ_{NH} = 3.04 and χ_{OH} = 3.44, that lead to the changes in bond strength on protonation. The plot for $A–F^+H$ seems to be linear for three of the points (dotted line in Figure 1, R^2 = 0.999) but levels off for $CH_3–F^+H$. This is not surprising since the electronegativity, $\chi_{FH}{}^+$ = 5.22 calculated from these three points, is extremely high. Thus the electronegativity difference, $|\chi_{CH_3} - \chi_{FH}{}^+|$ = 2.67, is so great that it has reached the saturation level discussed by Pauling[26] where the percent ionic character of the bond is approaching 90% and only increases slowly with increasing electronegativity difference.

A reviewer has suggested that the Pauling correlation between BDE and χ is unreliable. This is based on the observation that heats of reaction for eq 11, as calculated from electronegativity

$$AB + CD = AD + CB \quad (11)$$

$$\Delta H\ (\text{kJ mol}^{-1}) = 192(\chi_C - \chi_A)(\chi_B - \chi_D) \quad (12)$$

values (eq 12) do not agree in general with experimental values.[27] In fact in many cases ΔH(exptl) is negative and ΔH(calcd) is positive. However, over the relatively small range of hardness of the atoms reported here, eq 12 predicts ΔH quite reliably. There are 72 chemically unique permutations/combinations[28] of the fragments in the first column of Table I that can be substituted in eq 11. Therefore, ΔH(BDE) (evaluated from the calculated BDE) can be compared with $\Delta H(\chi)$ (evaluated from the electronegativities in Table II) to test eq 12. The results are plotted in Figure 2 where the line drawn is the ideal one of unit slope. The correlation is reasonable particularly when it is realized that the points that lie well below the line all contain the fragment F^+H from which the electronegativity ($\chi_{FH}{}^+$ = 5.22, Table II) is not reliably obtained by the Pauling method (vide supra). There are only two examples where ΔH is positive on one axis and negative on the other, but both these examples are very close to isothermal reactions.

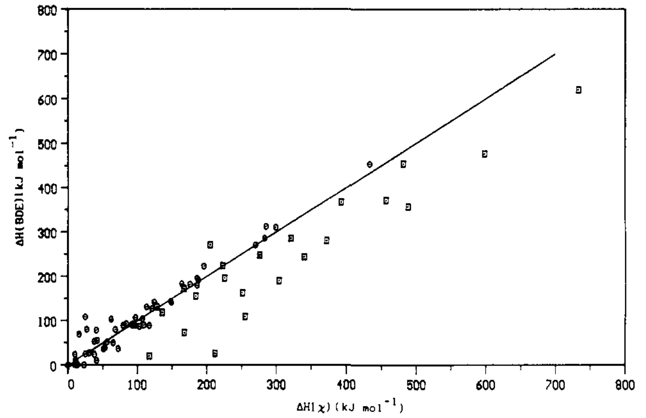


Figure 2. Graph of ΔH(BDE) versus $\Delta H(\chi)$. The line shown defines unit slope. Points shown as ⊡ are for cases that contain the fragment F^+H.

Three examples will suffice to show the way in which these changes in bond strength that result from protonation will have an influence on known chemical transformations. The first is that mentioned in the introduction to this paper. The bond strength for $(1\text{-}C_{10}H_7)CH_2–N(CH_3)_2$ can be estimated at about 247 kJ mol^{-1} on the basis of the known[29] value of 260 kJ mol^{-1} for $PhCH_2–N(CH_3)_2$ minus about 13 kJ mol^{-1} for stabilization of the 1-naphthylmethyl radical relative to that of benzyl.[30] Using our value of $\delta\Delta$ (128 kJ mol^{-1}, Table II) for protonation of a nitrogen attached to carbon gives an estimated value of 375 kJ mol^{-1} for the bond strength in $(1\text{-}C_{10}H_7)CH_2–N^+H(CH_3)_2$. The singlet excitation energy of naphthalene is 384 kJ mol^{-1} [31] so that bond cleavage from the excited singlet state will be exothermic and possible. The triplet excitation energy of naphthalene is only 255 kJ mol^{-1} [30] so that the bond cleavage is now endothermic and, as observed, should not occur. A similar analysis for $PhCH_2–O^+H_2$ gives a bond strength of 510 kJ mol^{-1}: 386 kJ mol^{-1} for $CH_3–OH$[29] minus 50 kJ mol^{-1} for benzylic stabilization in $PhCH_2–OH$ plus 174 kJ mol^{-1} (Table II) for $\delta\Delta$ of protonation of oxygen attached

---

(24) We have used the values[20] for the atoms C, N, and O rather than the groups CH_3, NH_2, and OH. Recent calculations[25] suggest there should be little difference between the two.

(25) Boyd, R. J.; Edgecombe, K. E. *J. Am. Chem. Soc.* **1988**, *110*, 4182.

(26) Reference 19; p 97.

(27) Pearson, R. G. *Chem. Commun.* **1968**, 65.

(28) This assumes that one, and only one, of the fragments is positively charged. Also conversions where two of the fragments are identical are included.

(29) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493.

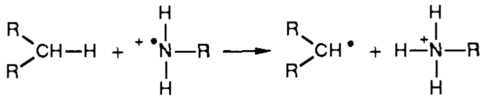
(30) Herndon, W. C. *J. Org. Chem.* **1981**, *46*, 2119.

(31) Turro, N. J. *Modern Molecular Photochemistry*; Benjamin/Cummings: Menlo Park, CA, 1978; p 352.

J. Am. Chem. Soc. **1989**, *111*, 5155–5165 5155

to carbon. The excitation energies of benzene[31] are 460 kJ mol^{-1} for the singlet and 351 kJ mol^{-1} for the triplet. As observed, homolytic excited-state bond cleavage should not occur.[4,5]

A second example is the free-radical chlorination of hydrocarbons by protonated *N*-chloroamines of which the intramolecular example is the Hofmann–Loffler–Freytag reaction.[32] Although there has been considerable dispute about the mechanism of these processes, it now appears to be well established that the critical chain-propagating step is hydrogen abstraction, often at a 2° carbon, by the radical cation of an amine (eq 13) Values of the BDE[29] for $(CH_3)_2CH–H$, 358 kJ mol^{-1}, and $H–N(CH_3)_2$, 383 kJ mol^{-1}, indicate that this step would be mildly exothermic for the neutral aminyl radical (eq 14). Protonation of the nitrogen increases the N–H bond strength and makes the step in eq 13 much more favorable.


(13)


(14)

As a third example,[13] we note the gas-phase elimination of H_2 from CH_3XH^+ (eq 15). In all cases, estimation of the activation energy for this process gives lower values than that calculated in this paper for homolytic cleavage of the strong C–X bonds.

$$CH_3XH^+ \rightarrow CH_2X^+ + H_2 \qquad X = NH_2, OH, F, SH \qquad (15)$$

Although our discussion has focused on the energetics of protonation, it is interesting to consider the changes, δr, in A–B bond lengths due to protonation. The data in Table III indicate that the trends for bond lengths are similar to those for bond dissociation energies. For example, δr, like $\delta\Delta$, increases along the series $CH_3–NH_2/CH_3–N^+H_3$, $CH_3–OH/CH_3–O^+H_2$, $CH_3–F/CH_3–F^+H$. In general, protonation leads to an increase in the A–B bond length, with three exceptions being noted among the HF/6-31G*-optimized structures included in this paper. Two of the three cases correspond to the two cases for which $\delta\Delta$ is also negative (see Table II). Normally, bond lengths decrease as bond strengths increase, and in fact correlations have been made between the shortening of bond lengths and the electronegativity difference of bonded atoms.[33] Although we do not have an explanation for this observation, the rather unusual lengthening of bonds despite the increased electronegativity is likely due to the positive charge on the heteroatom. The geometries of three of the pairs of molecules have been optimized using the MP2 method. The results listed in Table III indicate that including the effects of electron correlation does not alter the qualitative trends and, therefore, we conclude that the HF/6-31G*-optimized structures are sufficiently accurate for the present purposes.

Note Added in Proof. After this paper was accepted for publication we learned from Professor D. R. Arnold of a similar discussion of the relationship between bond dissociation energies and the electronegativity of charged atoms.[34]

Acknowledgment. We thank William Brandon for some preliminary calculations and the Natural Sciences and Engineering Research Council of Canada for financial assistance.

---

(32) Tanner, D. D.; Arhart, R. *Tetrahedron* **1985**, *41*, 4261, and references therein.

(33) Reference 19; pp 228–230.

(34) Williams, T. F. *J. Am. Chem. Soc.* **1962**, *84*, 2895.

Molecular Dynamics Simulations of α-D-Glucose in Aqueous Solution

J. W. Brady

Contribution from the Department of Food Science, Stocking Hall, Cornell University, Ithaca, New York 14853.
Received October 27, 1988

Abstract: Molecular dynamics simulations have been performed for an aqueous solution of α-D-glucopyranose. A single glucose molecule was modeled surrounded by 207 SPC water molecules using periodic boundary conditions in the microcanonical ensemble. Solvation was found to have little effect upon the dynamically averaged structure of the sugar molecule. Transitions in the orientations of the various carbohydrate hydroxyl groups, which were found to be extremely unlikely in vacuo, occurred easily in solution, although the rotational motions were damped by the solvent. The exocyclic hydroxymethyl group unexpectedly rotated spontaneously to the trans–gauche (TG) conformation early in the simulation and remained in this orientation for the remainder of the calculation. The structuring of the water molecules around the C2 hydroxyl group was found to be substantially perturbed for some orientations of this group relative to the anomeric hydroxyl group. This perturbation may be the result of inadequate averaging due to the simulation time scale or, if real, could be related to the basis for the differing anomeric concentrations at equilibrium.

I. Introduction

It is now generally understood that the conformational structure and dynamics of biopolymers are strongly influenced by aqueous solvation. Unfortunately, the role of water in these biological systems is not simple or easily generalized. The special behavior of aqueous systems, arising from the unique molecular structure and hydrogen-bonding properties of water, makes dielectric continuum models of aqueous solutions inadequate for understanding many important properties of biological molecules in solution. Furthermore, the complex chemical structure of most biological solutes makes such systems particularly difficult to treat theoretically; often quite different functional groups, such as nonpolar aliphatic groups and hydrogen-bonding dipoles, are juxtaposed in close spatial proximity in molecules such as peptides or nucleic acids. Fortunately, with the advent of high-speed computers, it is becoming feasible to use techniques such as Monte Carlo and molecular dynamics simulations[1-3] to directly model

---

(1) Brooks, C. L.; Karplus, M.; Pettitt, B. M. Proteins: A Theoretical Perspective of Dynamics, Structure, and Thermodynamics. *Advances in Chemical Physics* Wiley-Interscience: New York, 1988; Vol. LXXI.

(2) Karplus, M.; McCammon, J. A. *Annu. Rev. Biochem.* **1983**, *53*, 263.

0002-7863/89/1511-5155$01.50/0 © 1989 American Chemical Society