Prediction of Proton Affinities and Preferred Protonation Sites in Benzene Derivatives, from 1*s* Orbital Energies

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We have found a good linear correlation between the experimental proton affinity and the '*ab initio*' highest C_{1s} orbital energy, obtained using an STO–3G minimal basis set, for a wide set of benzene derivatives that are protonated on the ring. Similar relationships were found with the O_{1s} or the N_{1s} orbital energies for those compounds that are oxygen- or nitrogen-bases, respectively. This provides a simple method for the calculation of proton affinities and the classification of different centres according to their intrinsic basicity. A possible extension of this treatment to non-aromatic compounds is also discussed.

GAS-PHASE proton affinities can be measured with high accuracy by high-pressure mass spectroscopy,[1,2] ion cyclotron resonance,[3] and flowing-afterglow experiments.[4] The absence of solvation effects permits direct comparison of measured and calculated proton affinities. However, experimental determination of the preferred protonation site of a given molecule is seldom possible (some exceptions are some benzene derivatives where protonation sites can be determined by means of sequential deuterium exchange reactions [5]) and in most cases one must obtain this kind of information from theoretical calculations. In fact, considerable effort has been devoted to determine the preferred protonation site of some benzene derivatives from energy changes in the 'isodesmic' proton transfer reactions [6-9] or from molecular electrostatic potentials.[10,11]

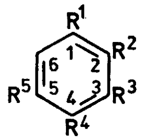
Recently, we have presented [11] a very simple way to evaluate proton affinities of monosubstituted benzene derivatives from the linear correlation we have found between experimental proton affinities and calculated 1*s* orbital energies of the *para*-carbon atom. The equation obtained can be used to predict proton affinities of the other positions (from the corresponding C_{1s} orbital energies).[12] This equation can also be used to decide on the preferred protonation sites of monosubstituted benzenes.

In this paper we test the application of this correlation to polysubstituted benzene derivatives. We have also found similar correlations between calculated O_{1s} and N_{1s} orbital energies and experimental proton affinities for those benzene derivatives that are oxygen- or nitrogen-bases.

Ring Proton Affinities.—We have selected the following benzene derivatives: *o*- (1), *m*- (2), and *p*-xylene (3), mesitylene (4), *m*-difluorobenzene (5), and 1,3,5-trifluorobenzene (6) because there is experimental evidence that they are protonated on the ring and data are available on their experimental proton affinities.[7,13,14] We have also included the results for benzene (7), toluene (8), and fluorobenzene [11] to show that just one equation can be used for any (mono- or poly-substituted) benzene derivatives.

To avoid time-consuming geometry optimizations we have used experimental geometries [15] and an STO-3G minimal basis set.[16]

We have found a good linear correlation between the experimental proton affinity of these compounds and the highest C_{1s} orbital energy (lowest 1*s* binding energy), which corresponds to the *para*-carbon atom in all monosubstituted benzene derivatives [(8), (9)], to position 3 in *o*-xylene (1), 2 in *m*-xylene (2), 4 in *m*-difluorobenzene (5), and to a non-substituted position in the other three compounds [(3), (4), (6)].



	R1	R2	R3	R4	R5
(1)	Me	Me	H	H	H
(2)	Me	H	Me	H	H
(3)	Me	H	H	Me	H
(4)	Me	H	H	H	Me
(5)	F	H	F	H	H
(6)	F	H	F	H	F
(7)	H	H	H	H	H
(8)	Me	H	H	H	H
(9)	F	H	H	H	H

The linear relationship obtained (Figure 1) is given by equation (1), where the experimental proton affinity

$$\text{P.A.} = 846.34\,E(C_{1s}) + 9\,518.64$$
$$(r = 0.998 \text{ and } \sigma_{\text{P.A.}} = 0.4 \text{ kcal mol}^{-1}) \qquad (1)$$

(P.A.) is in kcal/mol and the C_{1s} orbital energy $[E(C_{1s})]$ in atomic units.†

The difference between equation (1) and that reported in ref. 11 is greatly reduced when one does not include phenol and equation (2) is obtained; it is not clear that

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† 1 cal = 4.184 J; 1 a.u. of energy (hartree) = 4.3598×10^{-18} J.

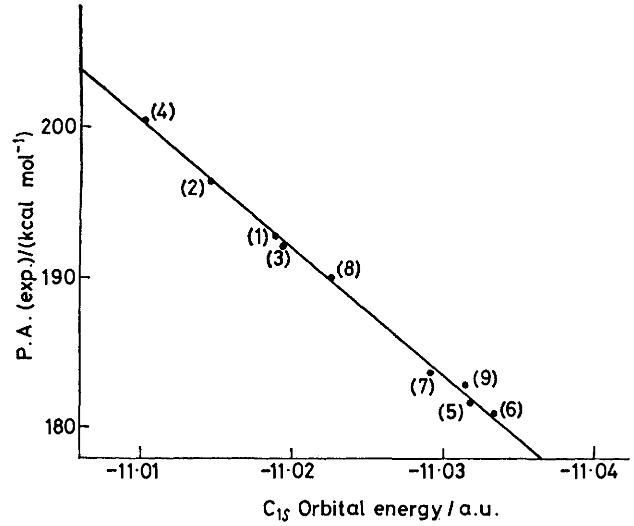

FIGURE 1 Correlation of experimental proton affinities and the highest C_1 orbital energies for benzene derivatives that are protonated on the ring

this compound is protonated on the ring. We shall discuss this problem later in more detail.

$$\text{P.A.} = 829.29\,E(C_{1s}) + 9\,330.72 \qquad (r = 0.987)\ * \qquad (2)$$

It is also interesting that, according to our results, *m*-xylene (2) should undergo protonation on position 2, in agreement with the conclusion reached by Freiser, Woodin, and Beauchamp[5] that *m*-xylene interchanges only a single proton in sequential deuterium exchange reactions. However, using equation (1), we have found a very small difference (0.8 kcal mol^{-1}) between the proton affinities of positions 2 and 4 and therefore to predict a protonation site one must take into account other factors, such as steric hindrance, that can influence the basicity of a given position.

We have also used equation (1) to predict ring proton affinities of benzene derivatives for which ring protonation is not well established or does not occur, using their experimental geometries the results obtained are in the Table. The first column corresponds to the highest C_{1s} orbital energy (*i.e.* to the most basic position of the ring). In all cases the theoretically predicted proton affinity is much smaller than the experimental one, indicating that protonation must take place on the substituents. These results include phenol, which was an ambiguous case in the previous study.[11] With equation (1), a ring proton affinity about 3 kcal mol^{-1} lower than the experimental one is predicted, confirming that phenol is not a ring-base.

As most of these compounds are oxygen- and nitrogen-containing molecules, it is reasonable to assume that they must be either oxygen- and nitrogen-bases, and this aspect is considered in the next section.

Oxygen- and Nitrogen-bases.—From the previous discussion we expect that oxygen- and nitrogen-containing benzene derivatives, which undergo protonation on the substituent, will show a linear relationship between their experimental proton affinities and the O_{1s} or N_{1s} orbital energies, respectively.

Theoretically predicted ring proton affinities (P.A.) of some benzene derivatives

Molecule	$E(C_{1s})$/a.u.[a]	Ring P.A. (theor.) kcal mol^{-1} [a]	P.A. (exp.) kcal mol^{-1} [a]
PhCHO (10)	−11.044 34	171.4	199.1 [b]
PhCN (11)	−11.059 00	159.0	195.1 [b]
$PhNO_2$ (12)	−11.064 56	154.3	192.6 [b]
PhOH (13)	−11.020 08	191.9	195.0 [b]
PhOMe (14)	−11.021 89	190.4	199.4 [b]
PhCOMe (15)	−11.036 01	178.4	203.1 [c]
$PhNH_2$ (16)	−11.011 15	199.5	208.8 [d]
p-$MeC_6H_4NH_2$ (17)	−11.019 45	192.5	211.6 [e]
m-$FC_6H_4NH_2$ (18)	−11.016 68	194.8	205.5 [e]
p-$FC_6H_4NH_2$ (19)	−11.027 81	185.4	206.4 [f]
$PhCH{=}CH_2$ (20)	−11.026 53	184.6	200.0 [g]

[a] 1 cal = 4.184 J; 1. a.u. of energy (hartree) = 4.3598 $\times 10^{-18}$ J. [b] Ref. 14. [c] B. S. Freiser and J. L. Beauchamp, *J. Amer. Chem. Soc.*, 1970, **98**, 265. [d] Ref. 8. [e] Ref. 9. [f] R. W. Taft, in 'Proton Transfer Reactions,' eds. E. F. Caldin and V. Gold, Wiley–Halstead, New York, 1975, ch. 2 p. 31. [g] Ref. 21.

To ensure that a reliable correlation is obtained for the oxygen-containing compounds, we have included three oxygen-bases that are not neutral molecules: the phenolate (21), *m*-hydroxyphenolate (22), and *m*-fluorophenolate (23)[17] anions. Nitrobenzene was not taken into account for reasons discussed elsewhere.[11]

$$\underset{(21)}{PhO^-} \qquad \underset{(22)}{m\text{-}HOC_6H_4O^-} \qquad \underset{(23)}{m\text{-}FC_6H_4O^-}$$

A least-squares fitting of the data (Figure 2) yields equation (3).

$$\text{P.A.} = 310.11\,E(O_{1s}) + 6\,488.68. \qquad (r = 0.999 \text{ and } \sigma_{\text{P.A.}} = 0.7 \text{ kcal mol}^{-1}) \qquad (3)$$

For nitrogen-bases (of the aniline type) experimental data are available for only four compounds [(16)—(19)],

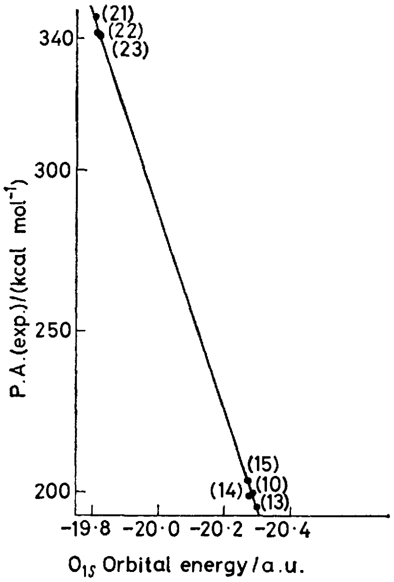

FIGURE 2 Experimental proton affinities *vs.* O_{1s} orbital energies for benzene derivatives that are oxygen-bases

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* Relationship for monosubstituted benzenes without including phenol.

which makes the linear correlation found [equation (4); Figure 3] less reliable than in the previous cases. However, when equation (4) is used to predict the proton affinity of other nitrogen-bases the results obtained are very reasonable, as we shall show in the next paragraph.

Equations (1), (3), and (4) can be used to evaluate in a very simple way the proton affinity associated with any ring-carbon, oxygen, or nitrogen atom in benzene derivatives. The results predicted for some of them, using once more their experimental geometries,[15] are given in Figure 4.

$$\text{P.A.} = 311.72\,E(\text{N}_{1s}) + 4\,987.48$$
$$(r = 0.982 \text{ and } \sigma_{\text{P.A.}} = 0.4 \text{ kcal mol}^{-1}) \qquad (4)$$

o- and *p*-Difluorobenzene are less basic than the *meta*-derivative (corresponding to the experimental findings in the case of the xylenes). Catechol is predicted to be oxygen-base, but resorcinol and phloroglucinol (similar to mesitylene) should be protonated on the ring. *m*- and *p*-Aminophenol are predicted to be nitrogen-bases (the latter being the stronger). It is interesting to note the difference in deactivation undergone by the positions of the aromatic ring for these two compounds, since in the latter all positions are always *meta* (and therefore of low activity) with respect to one of the substituents.

Qualitative Predictions.—As shown in the Table, styrene is not protonated on the ring and, in consequence, protonation must occur on a non-aromatic carbon atom. The question thus arises as to whether equation (1) applies to non-aromatic carbon atoms or to non-benzene rings. The correlation between proton affinities and 1*s* orbital energies, based on the assumption that the relaxation energy [18,19] (as a consequence of the removal of a core electron) is almost the same for the different ring positions,[12] seems to be quantitatively valid for compounds that belong to the same family. Of course, it is not obvious that the relaxation energy will be the same for non-aromatic carbon atoms, but if the change is not too significant, equation (1) could be used to estimate proton affinities at least qualitatively when protonation takes place on these carbon atoms and to predict the most basic one.

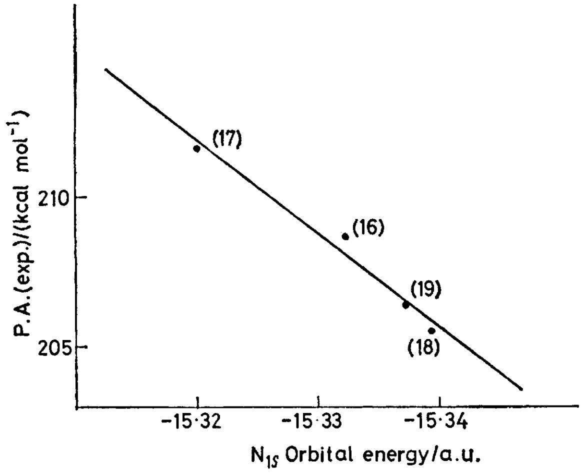

FIGURE 3 Experimental proton affinities *vs.* N_{1s} orbital energies for aniline derivatives

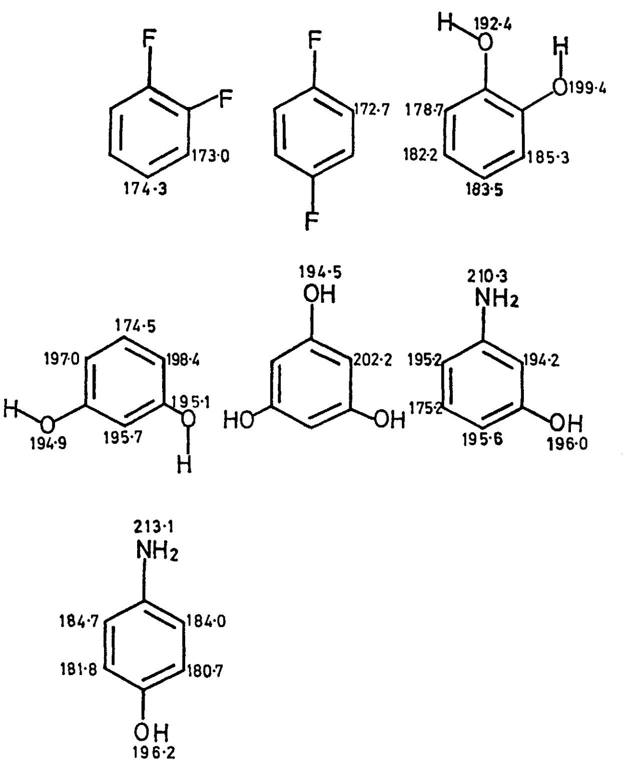

FIGURE 4 Proton affinities calculated using equations (1), (3), and (4), all values in kcal mol^{-1}

Application of equation (1) to styrene (20) (see Figure 5) indicates that this assumption is acceptable. Our results predict the CH_2 group as the most basic site of the molecule, in agreement with other theoretical calculations [20] and experimental evidence,[20] and the value of the theoretically estimated proton affinity is quite close to the experimental value [21] (200.0 kcal mol^{-1}).

We have also performed calculations on naphthalene, azulene, phenylacetylene, keten, formamide, *N*-methyl- and *NN*-dimethyl-formamide, and pyrrole, using experimental geometries. The last five compounds were included to test the predictive value of equations (3) and (4) for non-aromatic compounds containing oxygen and nitrogen atoms. Some of the results obtained are in Figure 5.

A similar basicity is predicted for both (α and β) positions of naphthalene. In the case of azulene, position 1 is the most basic one, in agreement with experimental results, and the proton affinity value estimated using equation (1) is, once more, very close to the experimental value [21] (223.2 kcal mol^{-1}).

For phenylacetylene the most basic position is the CH group (as in styrene) but, surprisingly, the estimated proton affinity is the highest of all compounds studied here (except azulene). It would be very interesting to investigate this experimentally.

Keten is predicted to undergo protonation on the CH_2 group, in agreement with experimental evidence [22] and other theoretical calculations.[23] Formamide, *N*-methyland *NN*-dimethyl-formamide, and pyrrole were reported by Cavell and Allison[24] to deviate significantly from the correlation between experimental proton affinities and experimental N_{1s} binding energies. According to our results, formamide and its *N*-methyl- and *NN*-dimethyl-derivatives are oxygen- and not nitrogen-bases, in agreement with the conclusions of these authors. For pyrrole, our equations predict the ring carbon atom β to nitrogen (see Figure 5) to be more basic than the nitrogen atom, which agrees with the assumptions of Cavell and Allison[24] and with other theoretical calculations.[25]

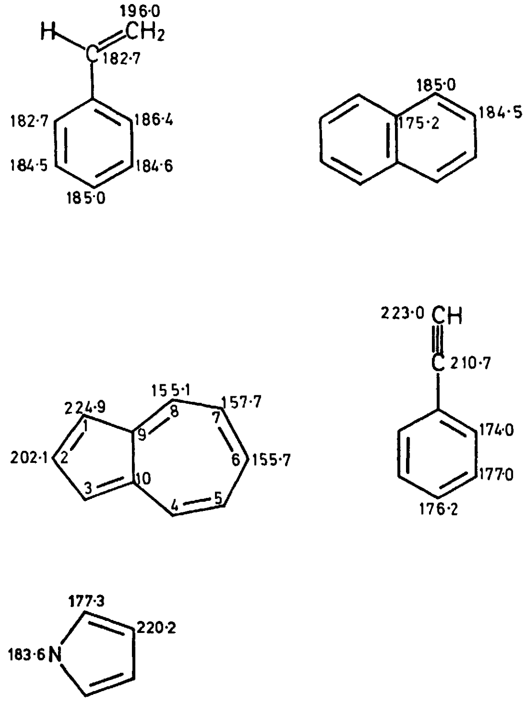

FIGURE 5 Proton affinities estimated using equations (1) and (4). All values in kcal mol^{-1}

NN-Dimethylaniline also deviates from the indicated correlation.[24] Since its experimental geometry is not known, we have adopted the ring structure of aniline, and for the substituent, the geometrical parameters of the *NN*-dimethylpyridine. Using this geometrical model, we have found that the deviation shown by this compound is due to the fact that protonation on the *para* carbon atom is much more favoured than nitrogen-protonation. Although this is a qualitative result, the difference between the estimated proton affinities is quite high (10 kcal mol^{-1}) and it is hard to believe that an improvement of the geometry would invert the basicities of these positions.

Conclusions.—We conclude from our results that the linear relationship between C_{1s} orbital energies and experimental proton affinities is applicable not only to monosubstituted benzene derivatives which are protonated on the ring, but to any kind of benzene derivative. Similar correlations between O_{1s} (and N_{1s}) orbital energies and experimental proton affinities of oxygen- (and nitrogen-) aromatic bases permit the calculation, in a very simple way, of proton affinities for this kind of compound, and the classification of the different centres according to their intrinsic basicity. As the differences in relaxation energy seem to be very small, these relationships can be used to estimate proton affinities and the most basic position of non-aromatic compounds.

All calculations were performed on the I.B.M. 360/65 computer at the U.A.M./I.B.M. Center (Madrid).

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REFERENCES

[1] J. P. Briggs, R. Yamdagni, and P. Kebarle, *J. Amer. Chem. Soc.*, 1972, **94**, 5128.

[2] R. Yamdagni and P. Kebarle, *J. Amer. Chem. Soc.*, 1976, **98**, 7452.

[3] M. T. Bowers, D. H. Aue, H. M. Webb, and R. T. McIver, jun., *J. Amer. Chem. Soc.*, 1971, **93**, 4314.

[4] D. K. Bohme, R. S. Hemsworth, R. S. Rundl, and H. W. Schiff, *J. Chem. Phys.*, 1973, **58**, 3504.

[5] B. S. Freiser, R. L. Woodin, and J. L. Beauchamp, *J. Amer. Chem. Soc.*, 1975, **97**, 6893.

[6] W. J. Hehre, R. T. McIver, jun., J. A. Pople, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1974, **96**, 7196.

[7] J. L. Devlin III, F. J. Wolf, R. W. Taft, and W. J. Hehre, *J. Amer. Chem. Soc.*, 1976, **98**, 1990.

[8] S. K. Pollack, J. L. Devlin III, K. D. Summerhays, R. W. Taft, and W. J. Hehre, *J. Amer. Chem. Soc.*, 1977, **99**, 4583.

[9] K. D. Summerhays, S. K. Pollack, R. W. Taft, and W. J. Hehre, *J. Amer. Chem. Soc.*, 1977, **99**, 4585.

[10] O. Chalvet, C. Decoret, and J. Royer, *Tetrahedron*, 1976, **32**, 2927.

[11] J. Catalán and M. Yáñez, *J.C.S. Perkin II*, 1979, 741.

[12] J. Catalán and M. Yáñez, *Chem. Phys. Letters*, 1979, **60**, 499.

[13] R. Yamdagni and P. Kebarle, *J. Amer. Chem. Soc.*, 1976, **98**, 1320.

[14] Y. K. Lau and P. Kebarle, *J. Amer. Chem. Soc.*, 1976, **98**, 7452.

[15] A. Langseth and B. P. Stoicheff, *Canad. J. Phys.*, 1956, **34**, 350; I. Takao, *Z. Naturforsch.*, 1977, **A32**, 1063; L. Nygaard, I. Bojensen, T. Pedersen, and J. Rastrup-Andersen, *J. Mol. Structure*, 1968, **2**, 209; T. Pedersen, N. W. Larsen, and L. Nygaard, *ibid.*, 1969, **4**, 59; J. Casado, L. Nygaard, and G. O. Sorensen, *ibid.*, 1971, **8**, 211; E. J. Schaick, H. J. Geise, F. C. Mijlhoff, and G. Renes, *ibid.*, 1973, **16**, 389; D. G. Lister, J. K. Tyler, J. H. Hog, and N. W. Larsen, *ibid.*, 1974, **23**, 253; J. Schlopf and A. Weber, *J. Raman Spectroscopy*, 1973, **1**, 3; H. D. Rudolf, K. Walzer, and I. Krutzik, *J. Mol. Spectroscopy*, 1973, **47**, 314; C. J. Brown, *Acta Cryst.*, 1951, **4**, 100; J. Trotter, *ibid.*, 1959, **12**, 884; K. Maartmann-Moe, *ibid.*, 1965, **19**, 155; Von H. Wünderlich and P. Mootz, *ibid.*, 1971, **B27**, 1684; D. Autona, F. Longcambon, M. T. Vanderborre, and P. Becker, *ibid.*, 1973, 1372; Y. Tanimoto, H. Kobayashi, S. Nayakura, and Y. Saito, *ibid.*, p. 1822; P. L. F. Jones, *Trans. Faraday Soc.*, 1935, **31**, 1036; G. Cazzoli, D. Domiani, and D. G. Lister, *J.C.S. Faraday II*, 1973, 119; A. P. Cox, I. C. Ewart, and W. Stigliani, *ibid.*, 1975, 504; L. Pauling and L. O. Brockway, *J. Amer. Chem. Soc.*, 1937, **59**, 1223; O. Bastiansen and J. L. Derissen, *Acta Chem. Scand.*, 1966, **20**, 1319; H. M. Seip and R. Seip, *ibid.*, 1973, **27**, 4024; R. K. Kadar, E. A. Rinehart, C. R. Quade, and T. Kojima, *J. Chem. Phys.*, 1970, **52**, 3803; J. Suhnel, K. Gustar, and P. Wild, *Z. Chem.*, 1977, **17**, 342; H. Oosaka, H. Sekine, and T. Saito, *Bull. Chem. Soc. Japan*, 1954, **27**, 182; A. Hatta, C. Hirosec, and K. Kojima, *ibid.*, 1968, **41**, 1088; G. E. Bacon and R. J. Jude, *Z. Krist.*, 1973, **138**, 19; C. De Rango, S. Brunie, G. Tsoucaris, J. P. Declerq, and G. Germain, *Cryst. Structure Comm.*, 1974, **3**, 485; L. E. Sutton, 'Interatomic Dstances,' The Chemical Society, London, 1965.

[16] W. J. Hehre, R. F. Stewart, and J. A. Pople, *J. Chem. Phys.*, 1969, **51**, 2657.

[17] T. B. McMahon and P. Kebarle, *J. Amer. Chem. Soc.*, 1977, **99**, 2222.

[18] R. L. Martin and D. A. Shirley, *J. Amer. Chem. Soc.*, 1974, **96**, 5299.

[19] B. E. Mills, R. L. Martin, and D. A. Shirley, *J. Amer. Chem. Soc.*, 1976, **98**, 2380.

[20] W. J. Hehre, in 'Modern Theoretical Chemistry, 4. Applications of Electronic Structure Theory,' ed. H. F. Schaefer III, Plenum Press, New York, 1977, ch. 7, p. 325.

[21] J. F. Wolf, P. G. Harch, and R. W. Taft, *J. Amer. Chem. Soc.*, 1975, **97**, 2904.

[22] J. Vogt, A. D. Williamson, and J. L. Beauchamp, *J. Amer. Chem. Soc.*, 1978, **100**, 3748.

[23] D. R. Yarkony and H. Schaefer III, *J. Chem. Phys.*, 1975, **63**, 4317.

[24] R. G. Cavell and D. A. Allison, *J. Amer. Chem. Soc.*, 1977, **99**, 4203.

[25] E. Scrocco and J. Tomasi, *Topics Current Chem.*, 1973, **42**, 95.