# A Theoretical Study of the Additivity of Proton Affinities in Aromatics: Polysubstituted Benzenes

Mirjana Eckert-Maksić, Martin Klessinger,* and Zvonimir B. Maksić*

**Abstract**: An additivity rule for proton affinities (PAs) in polysubstituted benzenes is derived from the MP2(fc)/6-31G**//HF/6-31G* + ZPE(HF/6-31G*) theoretical model by use of the concepts of homodesmic reactions and independent substituents. The performance of the additivity rule of thumb is very good; this is evidenced by the excellent agreement of the estimated PAs with the latest experimental data. We believe that the additivity should work for larger aromatic compounds too. The PA increments, which characterize the influence of each substituent on a particular site of the benzene ring undergoing electrophilic substitution, proved useful in discussing various chemical properties of this family of compounds.

**Keywords**
ab initio calculations · benzenes · electrophilic substitutions · proton affinities · QSAR

## Introduction

The investigation of gas-phase reactions has been an important development in the study of structure–reactivity correlations, since solvation effects are absent and the results are thus related to intrinsic reactivities.[1] The study of gas-phase acidities and basicities of molecules has been a major undertaking in this field for several decades.[2] Measurements of equilibrium constants for reversible proton transfer reactions [Eq. (1)] are used to determine gas-phase proton affinities (PAs).[3] Obviously, the PA of a molecule represents a fundamental thermodynamic property. In addition, protonation of aromatic molecules may be considered a model par excellence for the electrophilic substitution reaction,[4] yielding insight into the reaction mechanism,[5] and PAs of substituted benzene derivatives might be used to establish the intrinsic reactivity toward electrophilic substitution.

$$B_1H^+ + B_2 \rightleftharpoons B_1 + B_2H^+ \qquad (1)$$

Unfortunately, experimental techniques have some shortcomings in that absolute PA values are extremely difficult to determine. The use of Equation (1) led to various ladders of PA values dependent on the choice of the gauge base (anchor). As a consequence, the earlier values thus obtained were somewhat arbitrary. Moreover, measured PA values are usually related to the energetically most favorable protonation site and therefore yield little or no information about alternative sites of protonation. The theoretical approach, on the other hand, has the distinct advantage that all protonation sites are treated on the same footing, but a high level of theory is generally required for quantitative a priori estimates of PAs.

Although considerable progress has been made recently toward establishing an absolute scale of the proton affinities both in theoretical[6] and experimental[7] work, the G2 level of theory[8] is much too impractical for larger molecular systems, whereas the recent absolute scale of Szulejko and McMahon,[7] which has been cross-checked with high-level ab initio calculations, is still too limited to encompass numerous molecules of chemical interest. It is gratifying that a relatively simple model denoted by MP2(fc)/6-31G**//HF/6-31G* + ZPE(HF/6-31G*) is capable of providing PAs of good accuracy for medium-sized molecules, including substituted benzenes.[9, 10] Here ZPE denotes the zero-point vibrational energy, while other symbols have their usual meaning. Moreover, it was observed that PAs of difluorobenzenes and fluorotoluenes follow a simple additivity rule of thumb, which makes possible their estimation from the corresponding proton affinities of monosubstituted benzenes.[10]

In this paper we will derive an even simpler additivity formula that gives a new insight into the additivity relation, and show that the PAs of polysubstituted benzenes may be estimated from the PA of unsubstituted benzene plus increments $I(X)_\alpha$, which depend on the nature of the substituent X and the protonation site $\alpha$ (*ortho* (*o*), *meta* (*m*), *para* (*p*) and *ipso* (*i*), respectively). We extend the previous work a) to include disubstituted benzenes involving some other substituent groups (OH, CN) that differ considerably in their interactions with an aromatic moiety; b) to discuss the performance of the additivity "rule of thumb" in reproducing PAs of a large number of the trisubstituted benzenes; and c) to make some predictions concerning some heavily substituted benzenes. Theoretical estimates are

---

Organisch-Chemisches Institut der Westfälischen Wilhelms-Universität
Corrensstrasse 40, 48149 Münster (Germany)
Fax: Int. code + (251)83-9772
e-mail: klessim@uni-muenster.de

Prof. Dr. M. Eckert-Maksić, Prof. Dr. Z. B. Maksić
Department of Chemistry, Ruđer Bošković Institute
P. O. Box 1016, 10000 Zagreb (Croatia)
and
University of Zagreb
Marulićev trg 19, 10000 Zagreb-HR, Croatia
e-mail: zmaksic@spider.irb.hr, mmaksic@emma.irb.hr

0947-6539/96/0210-1252 $ 15.00+.25/0

compared with the available experimental data. In particular, it is shown that the PAs predicted by additivity rules are in good agreement with the most recent results of Szulejko and McMahon.[7] Finally, the possibility of designing better additivity rules is briefly discussed.

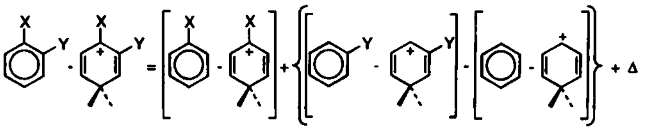
## Theoretical Method

**Method of computation**: Proton affinities are calculated with the general equation (2), where M and $M^+$ stand for the base in question and its conjugated acid,

$$\mathrm{PA}(\mathrm{M}_\alpha) = E(\mathrm{M}) + \mathrm{ZPE}(\mathrm{M}) - [E(\mathrm{M}_\alpha^+) + \mathrm{ZPE}(\mathrm{M}_\alpha^+)] \qquad (2)$$

respectively, and α denotes the site of the proton attack. The theoretical model we use here is the one that proved useful in calculating PAs of monosubstituted benzenes [9,10]. It involves optimization of all independent structural parameters at the HF/6-31 G* level and a test of the Hessian for the minimum on the potential energy surface. For OH-substituted benzenes several stable rotamers may exist; the results in Tables 3 and 4 (see below) refer to the global minimum, which usually corresponds to the same conformation of the OH group in the unprotonated and the protonated form, exceptions being the 6-protonated forms of 1-hydroxy-3-methylbenzene and 1-hydroxy-2,3-dimethylbenzene. The corresponding vibrational frequencies are used to extract the zero-point vibrational energies (ZPE). The latter are multiplied as usual by a common empirical factor, 0.89 [11]. The resulting total energies employed in Equation (2) are computed at the single point MP2(fc)//6-31 G**//HF/6-31 G* level in order to take into account explicitly a large portion of the electron correlation energy and provide a better description of the H atoms (G** basis set). Calculations were performed by the GAUSSIAN 94 programs [12].

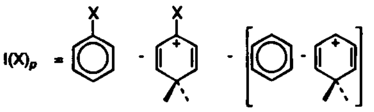
**PA increments**: Additivity of PAs in polysubstituted benzenes is easily derived by means of the concept of homodesmic chemical reactions [13], if it is assumed that the interaction between substituents is relatively small. The PA of a 1,2-substituted benzene, for instance, can be written as in Equation (3). Adding and substracting on the right-hand side the PA of benzene given by the last brackets yields Equation (4).



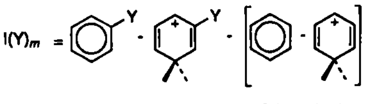
(3)

$$\mathrm{PA}(\mathrm{C_6H_4X_\mathit{p}Y_\mathit{m}}) = \mathrm{PA(benzene)} + I(\mathrm{X})_p + I(\mathrm{Y})_m + \Delta \qquad (4)$$

$I(\mathrm{X})_p$ and $I(\mathrm{Y})_m$ are used here to denote the increments defined in Equations (5a) and (5b), respectively. Obviously, the increments describe the change in the PA of benzene caused by the presence of the substituent at a particular position of the ring.

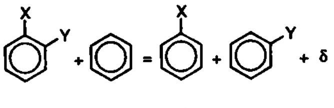


(5a)

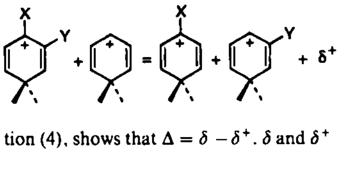


(5b)

If Δ in Equation (4) is negligible, PA values of polysubstituted benzenes can be estimated in an additive way simply from the corresponding increments. In order to see that Δ can in fact be expected to be small, let us consider the homodesmic reactions (6) and (7). After some rearrangement the difference Equation (6) − Equation (7) may be written as Equation (8), which, when compared with Equation (4), shows that $\Delta = \delta - \delta^+$.



(6)



(7)

$$\mathrm{PA}(\mathrm{C_6H_4X_\mathit{p}Y_\mathit{m}}) = \mathrm{PA(benzene)} + I(\mathrm{X})_p + I(\mathrm{Y})_m + (\delta - \delta^+) \qquad (8)$$

δ and $\delta^+$ measure the interaction between the two substituents X and Y in the unprotonated and protonated species, respectively, and are fairly small quantities; owing to the similarity in the bonding situations in Equations (6) and (7), δ and $\delta^+$ are expected to cancel to a large extent in Equation (8). Calculations demonstrate that this cancellation is surprisingly good, as evidenced by the actual values of Δ given in Tables 3 and 4. As a consequence, the additivity of substituent effects on the PA of benzene is in fact a very good approximation. The generalization of Equation (4) is straightforward. The PA of a multiply substituted benzene will then be given by Equation (9), where the summation runs over all substituents $N$, and $\alpha(N)$ denotes the position of the substituent relative to the protonation site ($\alpha = o, m, p, i$).

$$\mathrm{PA(subst.\ benzene)} = \mathrm{PA(benzene)} + \sum_N I(N)_{\alpha(N)} \qquad (9)$$

In Table 1, PA increments calculated according to Equation (5) are collected for four substituents, which differ widely in their interactions with the phenyl group: the $CH_3$ group is a weak σ- and π-electron donor, the OH and F substituents are σ acceptors and π donors, while the CN group has strong σ- and π-electron-withdrawing properties.

Table 1. Proton affinity increments $I(\mathrm{X})$ (in kcal mol$^{-1}$) for various positions of the benzene ring.

| Substituent | Increments [a] | | | |
|---|---|---|---|---|
| X | $I(\mathrm{X})_o$ | $I(\mathrm{X})_m$ | $I(\mathrm{X})_p$ | $I(\mathrm{X})_i$ |
| -$CH_3$ | 6.3 | 3.0 | 7.4 | 0 |
| -OH | 13.1 | 0 | 15.6 | −17.7 |
| -F | −0.5 | −7.4 | 1.7 | −23.2 |
| -C≡N | −13.1 | −15.9 | −13.2 | −23.0 |

[a] From PA(MP2) values for monosubstituted benzenes in ref. [9] (OH), ref. [10] ($CH_3$, F) and in ref. [26] (CN).

Table 2. Dependence of the PA increments $I(\mathrm{OH})$ on the theoretical model.

| Model | Increments [a] | | | |
|---|---|---|---|---|
| | $I(\mathrm{X})_o$ | $I(\mathrm{X})_m$ | $I(\mathrm{X})_p$ | $I(\mathrm{X})_i$ |
| HF/6-31 G* | 13.0 | −3.7 | 16.1 | −15.8 |
| MP2(fc)/6-31 G*//HF/6-31 G* | 12.8 | −0.4 | 15.3 | −18.2 |
| MP2(fc)/6-31 G**//HF/6-31 G* | 13.1 | 0.0 | 15.6 | −17.7 |
| MP2(fu)/6-311G*//HF/6-31 G* | 13.7 | 0.4 | 16.4 | −18.0 |

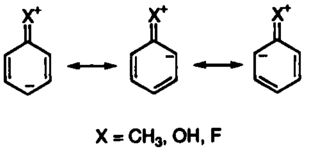
[a] From PA(MP2) values for phenol in ref. [9].

Calculated PA values depend very heavily on the theoretical model used [9,10]. PA increments, however, are quite insensitive and stable provided the MP2 model is used, while the HF/6-31 G* model usually fails for one or another position of the benzene ring. This is exemplified in Table 2 for the OH increments, which are obtained from PAs calculated by the HF/6-31 G* and MP2 model with different basis sets and HF/6-31 G* optimized structures [9].

## Results and Discussion

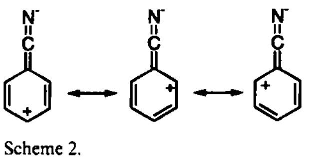
**Monosubstituted benzenes**: Before dealing with the additivity of PAs, we shall briefly discuss the PA increments of Table 1 and how they describe the changes in the electronic structure and reactivity of the benzene ring induced by the various substituents. In the following, it is assumed that Wheland intermediates[14] (σ complexes) formed by protonation describe fairly well the nearby transition state for the electrophilic substitution reaction, as suggested by Hammond's postulate.[15] Consequently, we may say that a particular position is more reactive relative to benzene if the PA increment is positive. The opposite holds for negative values of the PA increments.

The increments of the methyl group (Table 1) exhibit the following set of inequalities: $I(\mathrm{CH_3})_p > I(\mathrm{CH_3})_o > I(\mathrm{CH_3})_m > I(\mathrm{CH_3})_i = 0$; in other words, this substituent activates the *para*, *ortho*, and *meta* positions in agreement with the π-electron distribution described by the resonance structures depicted in



Scheme 1.

Scheme 1, whereas it has no effect on the *ipso* carbon, as has been noticed earlier.[16] The hydroxy group introduces the greatest degree of selectivity into electrophilic reactions; this is demonstrated by the $I(\mathrm{OH})_o$ and $I(\mathrm{OH})_p$ increments of 13.1 and 15.6 kcal mol$^{-1}$, respectively. As a peculiarity, we mention that *meta* positions remain unaffected, since $I(\mathrm{OH})_m = 0.0$. This finding is at variance with the common textbook statement that the *meta* position is slightly deactivated relative to benzene.[17] Both OH and F atom increments satisfy the inequalities $I(X)_p > I(X)_o > I(X)_m \gg I(X)_i$, where X = OH, F, but the activation of the *para* position by fluorine is very small. Nevertheless, it is about 1.7 kcal mol$^{-1}$, which is again contrary to the accepted contention that both *ortho* and *para* centers are deactivated relative to benzene in halobenzenes.[17] In fact, the energy profile curve for the electrophilic reaction in fluorobenzene should be split for *ortho* and *para* positions, the former lying above the free benzene curve and the latter below the calibration benzene curve. Our results are supported by the experimental measurements of Lau and Kebarle,[18] who studied a series of equilibrium proton transfer reactions at 600 K. The experimental $-\Delta H_f^\circ$ values relative to benzene were 1.3, 13.4, and 8.4 kcal mol$^{-1}$ for F-, OH-, and CH$_3$-substituted benzene derivatives, respectively. They are in fine agreement with the $I(X)_p$ increments for X = F, OH, and CH$_3$ (Table 1). Finally, it should be noted that the PA increments for OH and F substituents are compatible with the resonance structures depicted in Scheme 1.



Scheme 2.

In the case of the CN group the π-electron density pattern indicated by the resonance structures given in Scheme 2 is expected to be the opposite of the one discussed above, illustrating the fact that CN is a π-electron-withdrawing group. The increments $\Delta(\mathrm{CN})_\alpha$ ($\alpha = o, m, p, i$) follow this π-electron distribution insofar as all positions are deactivated. The deactivation of the *meta* position, however, is larger than that of the *ortho* and *para* positions, implying that the σ inductive effect is the overriding mechanism, since the experimental evidence shows that some electrophilic substituents prefer the *meta* position in cyanobenzene.[17] It follows that specific characteristics of the substituent in question should be explicitly taken into account. Nevertheless, it is important to know the PA increments, since a deviation in the behavior of a particular electrophilic substituent could be ascribed to the electronic properties of the attacking substituent.

Utilizing the proton as a probe of the electronic structure and reactivity of the phenyl ring, one is tempted to define its average stabilization or destabilization energy by summing up all but the *ipso* increments of the ring carbons, yielding Equation (10),

$$I(X)_{av} = \frac{1}{5}\sum_{\alpha \neq i} I(X)_\alpha \qquad (10)$$

where the summation runs over all positions of the phenyl fragment excluding the *ipso* position, and the total sum is divided by the number of terms in the sum. Protonation at the *ipso* position was omitted because it considerably perturbs the substituent itself and the C–X bond in view of the significant rehybridization (sp$^2$ → sp$^3$) at the site of attack. Hence, if the *ipso* increment were taken into account, $I(X)_{av}$ would involve changes imposed by the "measuring device" (the incoming proton), which have nothing to do with the effect of a substituent on the benzene ring. The $I(X)_{av}$ values obtained from Equation (10) are 5.2, 8.4, −2.8, and −15.3 kcal mol$^{-1}$ for CH$_3$, OH, F, and CN, respectively. It appears that an appreciable stabilization of the benzene ring by CH$_3$ and OH groups is predicted and F is a borderline case, whereas the CN group dramatically decreases the stability of the benzene ring.

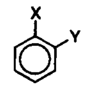
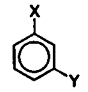
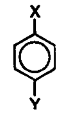
**Disubstituted benzenes**: The energetic data necessary for calculating PAs of disubstituted benzenes are collected in Table 3 together with theoretical MP2 and additivity PA values and the available experimental data. In the notation used here, the protonation site is defined relative to all substituents by the index α at each substituent. Together with the substitution pattern (e.g., 1,2,4-trisubstituted benzene $C_6H_3XYZ$) this fully identifies each species. In applying the additivity rule of Equation (9) we use the reference value PA(benzene) = 179.9 kcal mol$^{-1}$,[10] which is in excellent agreement with the recent experimental value PA = 180.0 kcal mol$^{-1}$,[7] together with the increments $I(X)_\alpha$ and $I(Y)_\beta$ ($\alpha$, $\beta = o, m, p$) given in Table 1. The average absolute deviation $|\Delta|_{av}$ between PA(MP2) and PA(add) is 1.0 kcal mol$^{-1}$, which illustrates the excellent performance of the additivity "rule of thumb" in view of the utmost simplicity of the independent-substituent model.

Since the additivity seemed to work well, our next task was to compare both sets of theoretical results with the experimental data. Unfortunately, the latter are sparse and if they are available for some systems, then there are usually several estimates, which sometimes differ widely depending on the PA ladder in question. It is encouraging that the PA scale of Szulejko and McMahon, anchored to the absolute proton affinity of CO, gives values in accordance with our predictions.[7] For example, for 4-protonated 1,2-difluorobenzene (1,2-$(\mathrm{F})_p$,$(\mathrm{F})_m$) the PAs estimated by the MP2 model and by the additivity rule differ greatly from earlier experimental data, but are in fine accordance with the results of Szulejko and McMahon[7] (Table 3). We are inclined to believe that the additivity rule will be valuable in interpreting experimental data, particularly in distinguishing protonated (deuterated) isomeric di- and polysubstituted benzenes in ICR spectroscopy,[19] and perhaps even in the discrimination between results originating from different PA scales. Some caution has to be exercised, however, since errors could sometimes be as large as 3 kcal mol$^{-1}$ (Table 3). These are related to dihydroxybenzenes. No attempt is made here to adjust the PA increments empirically, for reasons to be discussed later.

It is not the aim of this paper to review all the experimental work on the electrophilic reactivity studies related to substituted benzenes. However, some illuminating examples will be given. For instance, the relative rates of protodetritiation in trifluoroacetic acid for various positions in toluene and *o*, *m* and *p*-xylenes[17] are in qualitative agreement with the increase in PA for the corresponding ring carbon atoms given by the additivity rule.

Further, it is well known that *o*-cresol is substituted mainly *ortho* and *para* to the OH group and not to the CH$_3$ group. This is obvious from the increments given in Table 1. Substitutions *ortho* and *para* to the methyl group would imply that the OH group does not enter into play, since $I(\mathrm{OH})_m = 0.0$, in sharp contrast to the other positions, where the OH fragment contributes either 13.1 ($I(\mathrm{OH})_o$) or 15.6 kcal mol$^{-1}$ ($I(\mathrm{OH})_p$). The synergistic action of OH and methyl groups is reflected by the fact that *o*-cresol reacts with bromine about five times more rapidly than does phenol.[20]

Table 3. Total molecular energies $E$ (in a.u.) and zero-point vibrational energies ZPE (in kcal mol$^{-1}$), as well as MP2 values PA(MP2), additivity estimates PA(add) and experimental data for proton affitinities (PAs) of some disubstituted benzenes. $\Delta$ denotes the difference PA(MP2) – PA(add). (All PA values in kcal mol$^{-1}$.)

| X | Y | $E$(HF) [a] | ZPE(HF) [b] | $E$(MP2) [c] | PA(MP2) | PA(add) | $\Delta$ | Experiment |
|---|---|---|---|---|---|---|---|---|
| *o*-disubstituted benzenes | |  | | | | | | |
| $CH_3$ | $CH_3$ | –308.77662 | 93.2 | –309.87860 | – | – | – | |
| $(CH_3)_m$ | $(CH_3)_o$ | –309.10069 | 99.2 | –310.18937 | 189.0 | 189.2 | –0.2 | |
| $(CH_3)_p$ | $(CH_3)_m$ | –309.10374 | 99.4 | –310.19059 | 189.7 | 193.6 | –3.9 | 193.3 [d]; 188.0 [e] |
| OH | OH | –380.41296 | 65.2 | –381.57806 | – | – | – | |
| $(OH)_m$ | $(OH)_o$ | –380.74190 | 72.0 | –381.89730 | 193.5 | 193.0 | 0.5 | |
| $(OH)_p$ | $(OH)_m$ | –380.75182 | 72.4 | –381.90431 | 197.5 | 195.5 | 2.0 | |
| F | F | –428.39819 | 50.6 | –429.51749 | – | – | – | |
| $(F)_m$ | $(F)_o$ | –428.69143 | 57.0 | –429.80190 | 172.2 | 172.0 | 0.2 | |
| $(F)_p$ | $(F)_m$ | –428.69773 | 57.0 | –429.80658 | 175.0 | 174.1 | 0.9 | 181.8 [d]; 183.2 [e]; 175.7 [e] |
| OH | $CH_3$ | –344.59553 | 79.3 | –345.72891 | – | – | – | |
| $(OH)_m$ | $(CH_3)_o$ | –344.90961 | 85.0 | –346.03522 | 186.5 | 186.2 | 0.3 | |
| $(OH)_p$ | $(CH_3)_m$ | –344.93804 | 86.5 | –346.05620 | 198.2 | 198.5 | –0.3 | |
| $(OH)_m$ | $(CH_3)_p$ | –344.91581 | 85.4 | –346.03731 | 187.4 | 187.3 | 0.1 | |
| $(OH)_o$ | $(CH_3)_m$ | –344.92889 | 86.3 | –346.04938 | 194.4 | 196.0 | –1.6 | |
| *m*-disubstituted benzenes | |  | | | | | | |
| $CH_3$ | $CH_3$ | –308.77729 | 92.8 | –309.87815 | – | – | – | |
| $(CH_3)_o$ | $(CH_3)_o$ | –309.11024 | 99.2 | –310.19457 | 192.1 | 192.5 | –0.4 | |
| $(CH_3)_p$ | $(CH_3)_o$ | –309.11309 | 99.2 | –310.19632 | 193.3 | 193.6 | –0.3 | 195.9 [d]; 188.1 [e]; 175.7 [f] |
| $(CH_3)_m$ | $(CH_3)_m$ | –309.09575 | 99.2 | –310.18468 | 186.0 | 185.9 | 0.1 | |
| OH | OH | –380.41477 | 65.4 | –381.57652 | – | – | – | |
| $(OH)_o$ | $(OH)_o$ | –380.76220 | 72.7 | –381.91181 | 203.1 | 206.1 | –2.8 | |
| $(OH)_p$ | $(OH)_o$ | –380.76870 | 72.9 | –381.91696 | 206.1 | 208.6 | –2.5 | |
| $(OH)_m$ | $(OH)_m$ | –380.71152 | 71.0 | –381.87297 | 180.4 | 179.9 | 0.5 | |
| F | F | –428.39819 | 50.6 | –429.52376 | – | – | – | |
| $(F)_o$ | $(F)_o$ | –428.71093 | 57.3 | –429.81854 | 178.3 | 178.9 | –0.6 | |
| $(F)_p$ | $(F)_o$ | –428.71640 | 57.3 | –429.82300 | 181.0 | 181.1 | –0.1 | 181.5 [d]; 181.6 [e]; 180.0 [f] |
| $(F)_m$ | $(F)_m$ | –428.68355 | 56.4 | –429.79698 | 165.6 | 165.0 | 0.6 | |
| OH | $CH_3$ | –344.59564 | 79.0 | –345.72729 | – | – | – | |
| $(OH)_o$ | $(CH_3)_o$ | –344.93796 | 86.2 | –346.05472 | 198.3 | 199.3 | –1.0 | |
| $(OH)_p$ | $(CH_3)_o$ | –344.94415 | 86.3 | –346.05961 | 201.2 | 201.8 | 0.6 | |
| $(OH)_m$ | $(CH_3)_m$ | –344.90433 | 85.0 | –346.02897 | 183.3 | 182.9 | 0.4 | |
| $(OH)_o$ | $(CH_3)_p$ | –344.94104 | 86.1 | –346.05678 | 199.7 | 200.4 | –0.7 | |
| *p*-disubstituted benzenes | |  | | | | | | |
| $CH_3$ | $CH_3$ | –308.77709 | 92.8 | –309.87808 | – | – | – | |
| $(CH_3)_m$ | $(CH_3)_o$ | –309.10346 | 99.1 | –310.18954 | 189.1 | 189.2 | –0.1 | 192.0 [d]; 188 [e]; 191.8 [e] |
| OH | OH | –380.40950 | 65.1 | –381.57416 | – | – | – | |
| $(OH)_o$ | $(OH)_m$ | –380.74173 | 72.3 | –381.89331 | 193.1 | 193.0 | 0.1 | |
| F | F | –428.40370 | 50.6 | –429.52292 | – | – | – | |
| $(F)_m$ | $(F)_o$ | –428.69866 | 57.0 | –429.80786 | 172.4 | 72.0 | 0.4 | 181.2 [d]; 182.7 [e]; 171.5 [f] |
| OH | $CH_3$ | –344.59441 | 79.1 | –345.72687 | – | – | – | |
| $(OH)_o$ | $(CH_3)_m$ | –344.93224 | 86.2 | –346.05008 | 185.4 | 186.2 | –0.8 | |
| $(OH)_m$ | $(CH_3)_o$ | –344.90770 | 84.6 | –346.03116 | 195.6 | 196.0 | –0.4 | |

[a] Calculated with the HF/6-31G* model. [b] Estimated at the HF/6-31G* level with a common scaling factor of 0.89. [c] Calculated with the MP2(f)/6-31G**//HF/6-31G* model. [d] Ref. [21]. [e] Ref. [24] and references given therein. [f] Ref. [7].

As a final comment in this section we note that the average stabilization or destabilization energy $I(X)'_{av}$ [Eq. (11)], where

$$I(X)'_{av}(\text{disubst.}) = \frac{1}{4}\sum_{X}\sum_{\alpha \neq i,j} I(X)_\alpha \qquad (11)$$

the first summation runs over the two substituents at $C_i$ and $C_j$ and the second one over all unsubstituted positions of the benzene ring, yields correctly the most stable isomer of the neutral disubstituted benzenes, although the relative energies of the isomers are somewhat overestimated. In all cases the *m*-disubstituted benzene is the most stable isomer. There are, however, two notable exceptions: *o*-dihydroxybenzene and *o*-cresol. In both cases the *ortho* isomer is the most stable, presumably because of hydrogen bonding.

**Polysubstituted benzenes**: The results for polysubstituted benzenes are collected in Table 4. The average absolute deviation $|\Delta|_{av}$ between PA(MP2) and PA(add) values is 1.2 kcal mol$^{-1}$. This is somewhat higher than the average error in disubstituted benzenes, as expected in view of the larger number of substitutents. The overall performance of the simple additivity rule is, however, quite satisfactory. Comparison with available but scarce experimental information is of some interest. The agreement with the Szulejko–McMahon[7] experimental data for the protonation of polyfluorobenzenes, for instance, is excellent,

Table 4. Total molecular energies $E$ (in Hartree) and zero-point vibrational energies ZPE (in kcal mol$^{-1}$), MP2 values PA(MP2), additivity estimates PA(add), and experimental data for proton affinitities (PAs) of some polysubstituted benzenes. Δ denotes the difference PA(MP2) − PA(add). (All PA values in kcal mol$^{-1}$.)

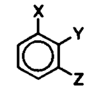
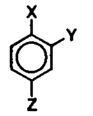
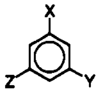
| X | Y | Z | $E$(HF) [a] | ZPE(HF) [b] | $E$(MP2) [c] | PA(MP2) | PA(add) | Δ | Experiment |
|---|---|---|---|---|---|---|---|---|---|
| 1,2,3-substituted benzenes | |  | | | | | | | |
| $CH_3$ | $CH_3$ | $CH_3$ | −347.80959 | 109.8 | −349.06361 | – | – | – | |
| $(CH_3)_p$ | $(CH_3)_m$ | $(CH_3)_o$ | −348.14614 | 116.1 | −349.38449 | 195.1 | 196.6 | −1.5 | |
| $(CH_3)_m$ | $(CH_3)_p$ | $(CH_3)_m$ | −348.14009 | 116.1 | −349.37978 | 192.1 | 192.1 | −1.2 | |
| F | F | F | −527.24102 | 45.8 | −528.51912 | – | – | – | |
| $(F)_p$ | $(F)_m$ | $(F)_o$ | −527.53722 | 52.5 | −528.80707 | 174.0 | 173.7 | 0.3 | 173.0 [f] |
| $(F)_m$ | $(F)_p$ | $(F)_m$ | −527.52526 | 52.2 | −528.79780 | 168.6 | 166.8 | 1.8 | |
| CN | $CH_3$ | F | −460.32579 | 71.2 | −461.70400 | – | – | – | |
| $(CN)_p$ | $(CH_3)_m$ | $(F)_o$ | −460.61287 | 77.4 | −461.98560 | 170.5 | 169.2 | 1.3 | |
| $(CN)_m$ | $(CH_3)_p$ | $(F)_m$ | −460.61229 | 76.9 | −461.97739 | 165.9 | 164.0 | 1.5 | |
| $(CN)_o$ | $(CH_3)_m$ | $(F)_p$ | −460.62043 | 77.6 | −461.98983 | 173.0 | 171.5 | 1.5 | |
| CN | F | $CH_3$ | −460.32479 | 71.3 | −461.70189 | – | – | – | |
| $(CN)_p$ | $(F)_m$ | $(CH_3)_o$ | −460.60533 | 76.8 | −461.97829 | 167.9 | 165.6 | 2.3 | |
| $(CN)_m$ | $(F)_p$ | $(CH_3)_m$ | −460.61843 | 77.6 | −461.98331 | 170.3 | 168.7 | 1.6 | |
| $(CN)_o$ | $(F)_m$ | $(CH_3)_p$ | −460.61225 | 77.2 | −461.98078 | 169.1 | 166.8 | 2.3 | |
| OH | $CH_3$ | $CH_3$ | −383.63012 | 95.8 | −384.91447 | – | – | – | |
| $(OH)_p$ | $(CH_3)_m$ | $(CH_3)_o$ | −383.98013 | 103.0 | −385.24943 | 203.0 | 204.8 | −1.8 | |
| $(OH)_m$ | $(CH_3)_p$ | $(CH_3)_o$ | −383.95303 | 102.1 | −385.22737 | 190.0 | 190.3 | −0.3 | |
| $(OH)_o$ | $(CH_3)_m$ | $(CH_3)_p$ | −383.97333 | 102.8 | −385.24437 | 200.1 | 202.3 | −2.2 | |
| 1,2,4-substituted benzenes | |  | | | | | | | |
| F | F | F | −527.24656 | 51.5 | −528.52466 | – | – | – | |
| $(F)_m$ | $(F)_o$ | $(F)_o$ | −527.53708 | 52.4 | −528.80781 | 171.1 | 171.5 | −0.4 | |
| $(F)_m$ | $(F)_p$ | $(F)_o$ | −527.54494 | 52.5 | −528.81420 | 175.0 | 173.7 | 1.3 | 183.4 [e]; 174.5 [f] |
| $(F)_o$ | $(F)_m$ | $(F)_m$ | −527.52473 | 52.0 | −528.79826 | 165.5 | 164.6 | 0.9 | |
| $CH_3$ | $CH_3$ | $CH_3$ | −347.81326 | 109.6 | −349.06544 | – | – | – | |
| $(CH_3)_m$ | $(CH_3)_o$ | $(CH_3)_o$ | −348.14744 | 115.7 | −349.38511 | 194.5 | 195.5 | −1.0 | |
| $(CH_3)_m$ | $(CH_3)_p$ | $(CH_3)_o$ | −348.15121 | 116.0 | −349.38684 | 195.3 | 196.6 | −1.3 | |
| $(CH_3)_o$ | $(CH_3)_m$ | $(CH_3)_m$ | −348.14116 | 115.8 | −349.38070− | 191.6 | 192.2 | −0.6 | |
| F | F | $CH_3$ | −467.43546 | 67.0 | −468.70430 | – | – | – | |
| $(F)_m$ | $(F)_o$ | $(CH_3)_o$ | −467.73984 | 73.3 | −468.99866 | 178.3 | 178.3 | 0.0 | |
| $(F)_m$ | $(F)_p$ | $(CH_3)_o$ | −467.74710 | 73.4 | −469.00418 | 181.7 | 180.5 | 1.2 | |
| $(F)_o$ | $(F)_m$ | $(CH_3)_m$ | −467.73302 | 73.4 | −468.99431 | 175.6 | 175.0 | 0.6 | |
| F | $CH_3$ | $CH_3$ | −407.62945 | 88.2 | −408.88980 | – | – | – | |
| $(F)_m$ | $(CH_3)_o$ | $(CH_3)_o$ | −407.94702 | 94.2 | −409.19469 | 185.2 | 185.1 | 0.1 | |
| $(F)_m$ | $(CH_3)_p$ | $(CH_3)_o$ | −407.95140 | 94.4 | −409.19373 | 186.9 | 186.2 | 0.7 | |
| $(F)_o$ | $(CH_3)_m$ | $(CH_3)_m$ | −407.94648 | 94.3 | −409.19602 | 186.1 | 185.4 | 0.7 | |
| $CH_3$ | $CH_3$ | OH | −383.63103 | 95.8 | −384.91442 | – | – | – | |
| $(CH_3)_m$ | $(CH_3)_o$ | $(OH)_o$ | −383.97408 | 102.4 | −385.24377 | 200.1 | 202.3 | −2.2 | |
| $(CH_3)_m$ | $(CH_3)_p$ | $(OH)_o$ | −383.97872 | 102.8 | −385.24639 | 201.7 | 203.4 | −1.7 | |
| $(CH_3)_o$ | $(CH_3)_m$ | $(OH)_m$ | −383.95079 | 101.7 | −385.22483 | 188.9 | 189.2 | −0.3 | |
| F | OH | $CH_3$ | −443.44498 | 74.4 | −444.73664 | – | – | – | |
| $(F)_m$ | $(OH)_o$ | $(CH_3)_o$ | −443.77196 | 81.2 | −445.05218 | 191.2 | 191.9 | −0.7 | |
| $(F)_m$ | $(OH)_p$ | $(CH_3)_o$ | −443.78156 | 81.5 | −445.05961 | 195.6 | 194.4 | 1.2 | |
| $(F)_o$ | $(OH)_m$ | $(CH_3)_m$ | −443.74977 | 80.6 | −445.03546 | 181.3 | 182.4 | −1.1 | |
| $CH_3$ | F | CN | −460.32659 | 71.2 | −461.70341 | – | – | – | |
| $(CH_3)_m$ | $(F)_o$ | $(CN)_o$ | −460.61570 | 77.6 | −461.98510 | 170.5 | 169.3 | 1.2 | |
| $(CH_3)_m$ | $(F)_p$ | $(CN)_o$ | −460.61959 | 77.6 | −461.98825 | 172.4 | 171.5 | 0.9 | |
| $(CH_3)_o$ | $(F)_m$ | $(CN)_m$ | −460.60902 | 76.8 | −461.97497 | 164.8 | 162.9 | 1.9 | |
| F | CN | $CH_3$ | −460.32343 | 71.1 | −461.69993 | – | – | – | |
| $(F)_m$ | $(CN)_o$ | $(CH_3)_o$ | −460.60861 | 77.1 | −461.97669 | 167.7 | 165.7 | 2.0 | |
| $(F)_m$ | $(CN)_p$ | $(CH_3)_o$ | −460.60464 | 76.8 | −461.97585 | 167.4 | 165.6 | 1.8 | |
| $(F)_o$ | $(CN)_m$ | $(CH_3)_m$ | −460.61282 | 77.4 | −461.97734 | 167.8 | 166.5 | 1.3 | |
| $CH_3$ | CN | F | −460.32491 | 70.4 | −461.70242 | – | – | – | |
| $(CH_3)_o$ | $(CN)_m$ | $(F)_m$ | −460.60883 | 76.8 | −461.97391 | 164.8 | 162.9 | 1.9 | |
| $(CH_3)_m$ | $(CN)_p$ | $(F)_o$ | −460.61180 | 77.4 | −461.98355 | 170.2 | 169.2 | 1.0 | |
| $(CH_3)_m$ | $(CN)_o$ | $(F)_o$ | −460.61580 | 77.5 | −461.98445 | 170.6 | 169.3 | 1.3 | |
| F | $CH_3$ | CN | −460.32784 | 71.3 | −461.70408 | – | – | – | |
| $(F)_m$ | $(CH_3)_o$ | $(CN)_o$ | −460.60933 | 76.9 | −461.97960 | 167.3 | 165.7 | 1.6 | |
| $(F)_m$ | $(CH_3)_p$ | $(CN)_o$ | −460.61233 | 77.0 | −461.98122 | 168.2 | 166.8 | 1.4 | |
| $(F)_o$ | $(CH_3)_m$ | $(CN)_m$ | −460.61602 | 77.5 | −461.98145 | 167.9 | 166.5 | 1.4 | |
| 1,3,5-substituted benzenes | |  | | | | | | | |
| F | F | F | −527.25511 | 45.8 | −528.53145 | – | – | – | |
| $(F)_p$ | $(F)_o$ | $(F)_o$ | −527.56152 | 52.7 | −528.82892 | 180.0 | 180.6 | −0.6 | 181.0 [d]; 178.4 [f] |
| $(F)_o$ | $(CH_3)_o$ | $(CH_3)_p$ | −626.08710 | 40.9 | −627.52463 | – | – | – | |
| $(F)_p$ | $(CH_3)_o$ | $(CH_3)_o$ | −626.36210 | 47.4 | −627.79673 | 164.2 | 164.1 | 0.1 | |

Table 4. (Continued)

| X | Y | Z | $E$(HF) [a] | ZPE(HF) [b] | $E$(MP2) [c] | PA(MP2) | PA(add) | Δ | Experiment |
|---|---|---|---|---|---|---|---|---|---|
| 1,2,3,4-tetrafluorobenzene | | | | | | | | | |
| | unprotonated | | −626.08166 | 41.0 | −627.51922 | – | – | – | |
| | 5-protonated | | −626.36450 | 47.6 | −627.79771 | 168.2 | 166.3 | 1.9 | 182.5 [e]; 181.1 [d]; 165.8 [f] |
| 1,2,4,5-tetrafluorobenzene | | | | | | | | | |
| | unprotonated | | −626.08710 | 40.9 | −627.52463 | – | – | – | |
| | 3-protonated | | −626.36210 | 47.4 | −627.79673 | 164.2 | 164.1 | 0.1 | |
| 1,2,3,4,5-pentafluorobenzene | | | | | | | | | |
| | unprotonated | | −724.92147 | 36.2 | −726.51805 | – | – | – | |
| | 6-protonated | | −725.20050 | 43.0 | −726.79463 | 166.8 | 165.8 | 1.0 | 182.4 [e]; 179.9 [d]; 164.3 [f] |
| hexafluorobenzene | | | | | | | | | |
| | unprotonated | | −823.75357 | 31.3 | −825.50979 | – | – | – | |
| | protonated | | −824.01424 | 38.7 | −825.76673 | 153.8 | 142.6 | 11.2 [g] | 180.5 [e]; 177.7 [d]; 153.8 [f] |

[a] Calculated with the HF/6-31G* model. [b] Estimated at the HF/6-31G* level with a common scaling factor of 0.89. [c] Calculated with the MP2(f)/6-31G**//HF/6-31G* model. [d] Ref. [21]. [e] Ref. [24] and references given therein. [f] Ref. [7]. [g] The new treatment of *ipso* protonation from ref. [22] yields PA(add) = 152.2 and Δ = 1.6.

giving strong support to the additivity of PAs in polysubstituted benzenes. On the other hand, agreement with the experimental data offered by older affinity ladders is much less satisfactory. The inconsistency of the PA values for these compounds was discussed earlier by Szulejko and McMahon.[7] For hexafluorobenzene a PA(add) value was obtained that was higher by 11 kcal mol$^{-1}$ than PA(MP2); this is by far the largest discrepancy for all systems considered. The very good performance of the additivity rule for tri-, tetra-, and pentafluorobenzenes (Table 4) suggested that the *ipso* protonation in hexafluorobenzene might be responsible for this deviation from additivity. This is indeed the case. The out-of-plane shift of the C–F bond leads to a strong interaction between substituent and ring orbitals that produces a considerable puckering of the benzene ring. Therefore, PA(benzene) is not an adequate reference level for calculating increments for *ipso* protonation, and PA($C_6H_5$–X)$_i$ should be employed instead. A modified treatment[22] offers a new PA(add) value for perfluorobenzene of 152.2 kcal mol$^{-1}$ in fine agreement with the MP2 result and experiment (Table 4).

For polymethylbenzenes not many experimental PA values are available, although Brown and Brady[23] determined the relative basicities of a number of aromatics including methylbenzenes. There is a very good proportionality between these relative basicities and the PA values obtained from the additivity rule, as illustrated in Figure 1. This proportionality demonstrates that the additivity works also for polymethylbenzenes, and also shows that in the case of these systems, solvent effects do not change the order of proton affinities or basicities. In addition, the additivity data supply theoretical relative basicities for durene and pentamethylbenzene, for which no experimental results are available, while for hexamethylbenzene PA(add) = 207.3 kcal mol$^{-1}$ agrees well with the experimental value of 206.2 kcal mol$^{-1}$.[2a, 24] It is interesting that, because $I(CH_3)_i = 0$, the predicted relative basicities are the same for penta- and hexamethylbenzene. An experimental confirmation of this finding would be desirable.

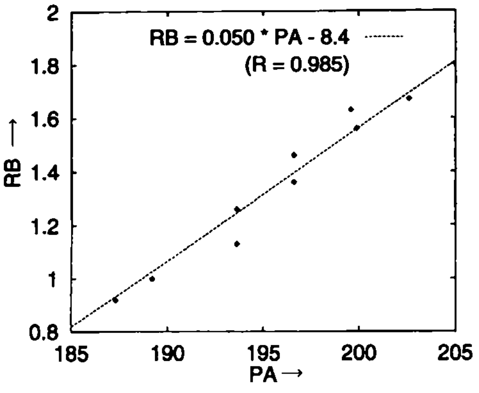


Fig. 1. Proportionality between relative basicities RB (ref. [23]) and proton affinities PA(add) of polymethylbenzenes.

As already discussed for disubstituted benzenes, the proton provides a useful probe of the electrophilic susceptibility of various ring positions. The well-known empirical *para* directive ability of halogens[25] is easily explained by the PA increments. For instance, the relative yields of 4- and 2-protonated 1-fluoro-3,5-dimethylbenzene are 84% and 16%, respectively.[25] The corresponding sums of the PA increments are 14.3 and 13.2 kcal mol$^{-1}$, respectively. The difference can indeed be ascribed to the activating (*para*) and deactivating (*ortho*) action of the F atom, since the methyl groups themselves favor protonation in position 2. This example illustrates rather nicely how the additivity concept can describe and quantify—albeit approximately—the interplay of various atomic groups in determining the chemical properties of the benzene ring.

## Conclusion

It has been shown by MP2(fc)/6-31G**//HF/6-31G* + ZPE(HF/6-31G*) calculations that the proton affinities of the ring carbons in polysubstituted benzenes are very well reproduced by additivity rules that require a simple algebra involving a few numbers, these being the increments $I(X)_o$, $I(X)_m$, $I(X)_p$, and $I(X)_i$ describing the effect of a particular substituent X on the various positions α (α = *o, m, p, i*) of the benzene ring. The additivity rule of thumb is based on the independent-substituent concept and rationalized by the relevant homodesmic reaction. The resulting PAs are strongly supported by good agreement with the latest absolute proton affinity scale.[7] The overall performance of the additivity is very good; however, deviations from the full MP2 calculations might be as large as 3 kcal mol$^{-1}$ in some rare cases. These errors could be "smoothed" by introducing the concept of effective increments. This is not done here because the aim of the present paper is to show that additivity works in principle. Development of effective increments requires calculations of PAs in more systems and consideration of neighboring-group effects. Experimental effective increments would be also very useful and could be obtained by careful examination of selected target molecules. We feel confident that the additivity concept is not confined to benzene only, but applies to all aromatic compounds.

PAs estimated by the additive rules may prove useful in interpreting a large body of experimental data. In particular, the sum of increments of all substituents for a particular site in the benzene ring offers an interesting insight into the synergistic or antagonistic interplay of various substituents in determining the electrophilic reactivity. We would like to stress that the proton is an interesting probe of the electronic structure, providing a reference scale for the electrophilic substitution process. Any deviations exhibited by a different incoming substitution group should be interpreted solely as the *differentia specifica* of this particular group, caused by its own electronic structure. As a useful application of the PA increments in rationalizing chemical properties of polysubstituted benzenes, a good correlation with the relative basicity of methylated benzenes should be mentioned.

**Acknowledgements**: M. E. M. and Z. B. M. would like to thank the Alexander von Humboldt-Stiftung and the Forschungszentrum Jülich GmbH, respectively, for financial support during their stay at the Organic Chemistry Institute of the University of Münster. Services and computer time of HLRZ Jülich are gratefully acknowledged.

Received: March 25, 1996 [F331]

---

[1] a) E. M. Arnett, *Acc. Chem. Res.* **1973**, *7*, 404; b) M. Meot-Ner (Mautner), *Acc. Chem. Res.* **1984**, *17*, 186; c) F. Cacace, *Acc. Chem. Res.* **1988**, *21*, 215.

[2] a) S. G. Lias, J. F. Liebman, R. D. Levin, *J. Phys. Chem. Ref. Data* **1984**, *13*, 695; b) G. A. Harrison, *Chemical Ionization Mass Spectrometry*, CRC, Boca Raton, **1989**.

[3] D. H. Aue, M. T. Bowers in *Gas Phase Ion Chemistry, Vol. 2* (Ed.: M. T. Bowers), Academic Press, New York, **1979**.

[4] R. Taylor, *Electrophilic Aromatic Substitution*, Wiley, Chichester, **1990**.

[5] M. Eckert-Maksić, Z. B. Maksić, M. Klessinger, *Int. J. Quant. Chem.* **1994**, *49*, 383; *J. Chem. Soc. Perkin Trans. 2*, **1994**, 285.

[6] B. J. Smith, L. Radom, *J. Am. Chem. Soc.* **1993**, *115*, 4885.

[7] J. E. Szulejko, T. B. McMahon, *J. Am. Chem. Soc.* **1993**, *115*, 7839.

[8] L. A. Curtiss, K. Raghavachari, G. W. Trucks, J. A. Pople, *J. Chem. Phys.* **1991**, *94*, 7221.

[9] M. Eckert-Maksić, M. Klessinger, Z. B. Maksić, *Chem. Phys. Lett.* **1995**, *232*, 472.

[10] M. Eckert-Maksić, M. Klessinger, Z. B. Maksić, *J. Phys. Org. Chem.* **1995**, *8*, 435.

[11] J. W. Hehre, L. Radom, P. v. R. Schleyer, J. A. Pople, *Ab Initio Molecular Orbital Theory*, Wiley-Interscience, New York, **1986**, and references cited therein.

[12] a) GAUSSIAN 92, Revision B, M. J. Frisch, G. W. Trucks, M. Head-Gordon, P. M. W. Gill, M. W. Wong, J. B. Foresman, B. G. Johnson, H. B. Schlegel, M. A. Robb, E. S. Replogle, R. Gomperts, J. L. Andres, K. Raghavachari, J. S. Binkley, C. Gonzalez, R. L. Martin, D. J. Fox, D. J. Defrees, J. Baker, J. J. P. Stewart, J. A. Pople, Gaussian, Pittsburgh PA, **1992**; b) GAUSSIAN 94, Revision B.2, M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanavakkara, M. Challacombe, C. Y. Peng, P. A. Avala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez, J. A. Pople, Gaussian, Pittsburgh PA, **1995**.

[13] P. George, M. Trachtmann, C. W. Bock, A. M. Brett, *Tetrahedron* **1976**, *32*, 313; *J. Chem. Soc. Perkin Trans. 2* **1976**, 1222.

[14] G. W. Wheland, *J. Am. Chem. Soc.* **1942**, *64*, 900.

[15] G. S. Hammond, *J. Am. Chem. Soc.* **1955**, *77*, 334.

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

[17] A. Streitwieser, Jr., C. H. Heathcock, *Introduction to Organic Chemistry*, Ch. 29, McMillan, New York, **1976**.

[18] Y. K. Lau, P. Kebarle, *J. Am. Chem. Soc.* **1976**, *98*, 7452.

[19] B. S. Freiser, R. L. Woodin, J. L. Beauchamp, *J. Am. Chem. Soc.* **1975**, *97*, 6893.

[20] P. B. D. De la Mare, *Tetrahedron* **1959**, *5*, 107.

[21] S. G. Lias, J. E. Bartmess, J. F. Liebman, J. L. Holmes, R. D. Levin, W. G. Mallard, *J. Phys. Chem. Ref. Data, Suppl. 1* **1988**, *17*.

[22] Z. B. Maksić, M. Eckert-Maksić, M. Klessinger, Chem. Phys. Lett. **1996**, in press.

[23] H. C. Brown, J. D. Brady, *J. Am. Chem. Soc.* **1952**, *74*, 3570.

[24] R. Walder, J. L. Franklin, *Int. J. Mass. Spectr. Ion Phys.* **1980**, *36*, 85.

[25] G. A. Olah, Y. K. Mo in *Carbonium Ions, Vol. 5* (Eds.: G. A. Olah, P. v. R. Schleyer), Wiley-Interscience, New York, **1976**, p. 2135.

[26] M. Eckert-Maksić, M. Hodošček, D. Kovaček, Z. B. Maksić, *J. Mol. Struct. (Theochem)*, **1996**, in press.