# Gas Phase Basicity of Substituted Benzaldehydes and Methylbenzoates. A Semiempirical Molecular Orbital Study

Walter Fabian
Institute of Organic Chemistry, University of Graz, Austria

Z. Naturforsch. **43a**, 85–90 (1988); received November 4, 1987

The semiempirical AM1 method is used to calculate relative proton affinities of a series of meta- and para-substituted benzaldehydes and methylbenzoates. Close agreement between the results of these calculations and experimental relative gas phase basicities could be obtained. The influence of a substituent on the stability of both neutral as well as protonated forms is estimated via isodesmic reactions. In any case the influence of a substituent is most pronounced in the protonated carbonyl compound. The contribution of the inductive/field effect of a substituent is approximated by the results of isolated molecule calculations. The resonance contribution is estimated by the charge transfer to or from the substituent as revealed by a Mulliken population analysis. Alternatively, the difference between isodesmic stabilization energies and isolated molecule results for the protonated compounds is taken as a measure for the resonance effect. Linear regression analyses with these substituent parameters show good correlation with both experimental as well as calculated relative basicities of the compounds studied.

## Introduction

Gas phase proton transfer reactions offer the unique opportunity to study intrinsic substituent effects on rates and equilibria of chemical reactions without complications due to solvent participation [1–6]. A few examples may serve to illustrate the pronounced solvent effects: Benzaldehyde is more basic in the gas phase than tetrahydrofuran; solvation by a single acetonitrile molecule is already sufficient to reverse this basicity order [5]. Both aniline and pyridine have been found to be more basic than ammonia in the gas phase contrary to results in solution [7]. In solution p-dimethylaminoacetophenone is protonated on the nitrogen atom whereas in the gas phase the carbonyl oxygen is the preferred site of protonation [1]. Finally, the well known Baker-Nathan series of the effect of alkyl groups on the acidity of alcohols has been shown to be completely reversed in the gas phase [8]. Thus, to establish unperturbed scales for substituent effects gas phase measurements are necessary. In addition such experiments are directly comparable to theoretical calculations. Provided a sufficient accurate method is chosen, quantum chemical computations should present valuable complements to experimental investigations.

In this paper we present semiempirical molecular orbital calculations using AM1 [9] on the gas phase basicities of a series of meta- and para-substituted benzaldehydes and methylbenzoates. These compounds have been selected because reliable experimental gas phase data for a sufficient variety of substituents are available [2, 4]. Furthermore, the expected ability of the methoxy group in the methylbenzoates to stabilize the positive charge in the protonated compounds offers the possibility to investigate the role of substituents in systems with different electron demand of the reaction centre. Thus, a comparison between the two sets of molecules should provide a more detailed insight into substituent effects.

## Calculational Details

All computations were performed with the semiempirical AM1 method [9]. This model has been chosen mainly for two reasons: (i) AM1 calculated proton affinities and deprotonation energies are comparable to results of medium to high level ab initio calculations [10]. (ii) Substituent effects (i.e. electron releasing or accepting ability) may critically depend on the conformation (torsion around essential single bond) of the substituent. In contrast to MNDO, which completely fails in this connection (e.g. the most stable conformations of benzaldehyde and nitrobenzene are predicted to be the perpendicular arrangements [9]), AM1 per-

---

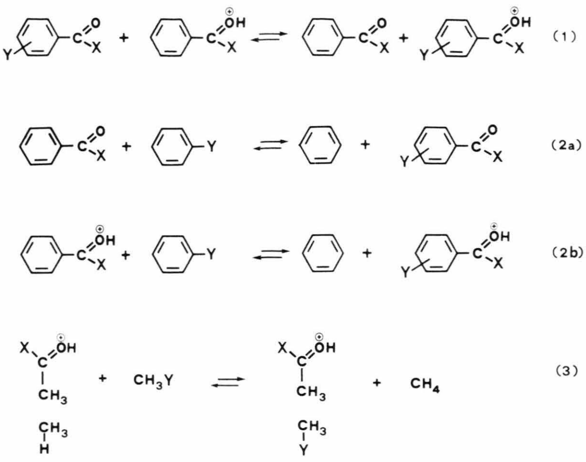
Reprint requests to Doz. Dr. Walter Fabian, Institute of Organic Chemistry, University of Graz, Heinrichstr. 28, A-8010 Graz, Austria.

0932-0784 / 88 / 0100-0085 $ 01.30/0. – Please order a reprint rather than making your own copy.

forms quite successfully in conformational problems [9, 11, 12]. Except for planarity of aromatic rings all other geometrical parameters were optimized without any further restriction.

Relative gas phase basicities were obtained via (1) in scheme 1 ($X = H, OCH_3$). Strictly speaking, experimental values correspond to changes in $\Delta G^0$ whereas the calculations refer to $\delta\Delta H^0$ values (i.e. relative proton affinities instead of basicities). However, changes in $\Delta S$ (mainly due to rotational symmetry numbers [13, 14]) should be small. In fact, it has been found that $\delta\Delta G^0$ values at both 298 K and 343 K are equal within experimental uncertainties [1]. Thus, both sets of data ($\delta\Delta G^0$ and $\delta\Delta H^0$) should be comparable.

Substituent effects on both neutral as well as protonated compounds are evaluated using isodesmic reactions [6, 15–17] ((2a) and (2b) in Scheme 1). Clearly, the difference between the heats of reaction obtained for (2a) and (2b) equals the calculated relative proton affinity as described by (1). To quantify substituent effects, generally dual substituent parameter treatments (inductive/field and resonance contributions, respectively) are employed [1–4, 6, 15, 16]. From a theoretical point of view the inductive/field contribution to substituent constants can be evaluated via isolated molecule calculations ((3) in Scheme 1) [6, 18–21]. In these calculations the same geometry (distance and orientation) of the C–Y bond relative to the carbonyl group in the $YCH_3/CH_3CXOH^+$ pairs is maintained as in the substituted benzaldehydes and methylbenzoates.



## Results and Discussion

Calculated relative proton affinities $\delta\Delta H^0$, (1), as well as substituent stabilization energies for neutral ($\Delta H(B)$), (2a), and protonated ($\Delta H(BH^+)$), (2b), benzaldehydes and methylbenzoates are compiled in Table 1. Also listed are the experimental relative gas phase basicities $\delta\Delta G^0$ (all values in kcal mol$^{-1}$). According to (1) a negative sign thus corresponds to a greater basicity of the substituted compound relative to the unsubstituted one. Similarly, a negative sign of both $\Delta H(B)$ as well as $\Delta H(BH^+)$ indicates stabilization by the substituent.

Table 1. Isodesmic stabilization energies $\Delta H(B)$ and $\Delta H(BH^+)$ for neutral and protonated compounds, calculated relative proton affinities $\delta\Delta H^0$, and experimental gas phase basicities $\delta\Delta G^0$ (in kcal mol$^{-1}$).

| Y | Benzaldehydes (**A**) | | | | Methylbenzoates (**B**) | | | |
|---|---|---|---|---|---|---|---|---|
| | $\Delta H(B)$ | $\Delta H(BH^+)$ | $\delta\Delta H$ | $\delta\Delta G$ [2] | $\Delta H(B)$ | $\Delta H(BH^+)$ | $\delta\Delta H$ | $\delta\Delta G$ [4] |
| H, **1** | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| m–OH, **2** | 0.4 | 2.0 | 1.6 | –0.5 | 0.5 | 1.4 | 0.9 | 0.2 |
| m–$NO_2$, **3** | 1.4 | 13.6 | 12.2 | 8.4 | 1.8 | 12.1 | 10.2 | 8.4 |
| m–$CH_3$, **4** | –0.1 | –1.2 | –1.2 | –2.8 | 0.0 | –1.1 | –1.1 | –1.4 |
| m–$CH_3O$, **5** | 1.0 | 0.8 | –0.2 | –2.7 | 0.4 | –0.1 | –0.5 | –1.5 |
| m–CN, **6** | 0.8 | 7.8 | 6.9 | 7.6 | 1.0 | 7.0 | 6.0 | 7.9 |
| p–$NO_2$, **7** | 2.1 | 16.4 | 14.2 | 8.7 | 2.4 | 14.2 | 11.9 | 8.9 |
| p–CHO, **8** | 1.0 | 6.6 | 5.6 | 4.5 | 1.2 | 5.8 | 4.6 | 4.2 |
| p–CN, **9** | 1.1 | 8.2 | 7.0 | 8.0 | 1.2 | 7.6 | 6.3 | 8.1 |
| p–$NH_2$, **10** | –1.2 | –16.2 | –15.0 | –13.0 | –1.5 | –11.9 | –10.3 | –8.0 |
| p–$CH_3O$, **11** | –0.1 | –6.4 | –6.2 | –10.2 | –0.8 | –4.6 | –3.8 | –4.8 |
| p–$CH_3$, **12** | –0.3 | –3.3 | –3.0 | –4.5 | –0.3 | –2.2 | –1.9 | –2.3 |
| p–OH, **13** | –0.7 | –4.7 | –4.0 | –6.9 | –0.7 | –2.8 | –2.1 | –3.1 |
| p–$N(CH_3)_2$, **14** | –2.0 | –19.4 | –17.4 | –21.1 | – | – | – | – |
| p–$CO_2CH_3$, **15** | – | – | – | – | 1.3 | 5.9 | 4.6 | 1.7 |

Except for m-hydroxybenzaldehyde, which is predicted somewhat too less basic, the agreement between calculated and experimental basicities is excellent. Good agreement is also found with ab initio calculations on relative proton affinities (in kcal mol$^{-1}$) of some of the benzaldehydes listed in Table 1: **3**: 11.7, **4**: −1.3, **5**: 0.5, **6**: 8.9, **7**: 14.1, **9**: 9.6, **10**: −12.2, **11**: − 8.8, **12**: − 4.0 [15]. In complete agreement with experimental findings [1] the carbonyl oxygen is predicted to be the preferred protonation site rather than the amino nitrogen atom in the amino-substituted derivatives **A-10, A-14,** and **B-10.** Protonation of the latter is calculated to be less favourable by 8–9 kcal mol$^{-1}$. **A-15** is identical with **B-8**. In the experimental investigation [4] protonation of the ester rather than the aldehyde group seems to have been assumed. This appears quite reasonable since methylbenzoate is found to be more basic than benzaldehyde by 3.6 kcal mol$^{-1}$ [2] (2.9 kcal mol$^{-1}$ according to [5]). AM1 yields a value of 3.9 kcal mol$^{-1}$ for this quantity. Consequently, protonation in p-CHO-methylbenzoate preferentially should occur at the ester group (according to the AM1 results favoured by 4.6 kcal mol$^{-1}$).

Furthermore, from the data of Table 1 it can be seen that the influence of substituents is most pronounced in the protonated forms. This is in complete agreement with previous findings for anilines and pyridines [6, 17]. Indeed, $\Delta H\,(\mathrm{BH}^+)$ values show good to excellent correlations with either $\delta\Delta G^0$ (benzaldehydes: $r = 0.971$; methylbenzoates: $r = 0.961$) or $\delta\Delta H^0$ (benzaldehydes: $r = 0.999$; methylbenzoates: $r = 0.999$; see Figure 1).

Consequently, in the following discussion we will focus our attention primarily on the substituent effects on the protonated compounds. As has been stated in the previous section, the inductive/field effect of a substituent may be estimated via isolated molecule calculations ((3) in Scheme 1). The results of these calculations ($\Delta H_{\mathrm{IM}}(\mathrm{BH}^+)$) are listed in Table 2. The resonance contribution may be approximated by the amount of charge transfer to or from the substituent [19–22]:

$$\sum \Delta q_\pi = n_\pi - \sum q_\pi ,$$

where $n_\pi$ is the number of $\pi$-electrons in the unsubstituted molecules. A negative sign thus corresponds to electron donation and a positive sign to electron withdrawal by the substituent. Values of $\sum \Delta q_\pi$ for the protonated species (obtained by a Mulliken population analysis) are also listed in Table 2. It is interesting to note that on the basis of these values the para-cyano group (**A-9, B-9**) should act as a weak electron donor. This agrees with previous findings that the electron attracting or releasing properties of substituents strongly depend on the electron demand of the reaction centre. Thus in strongly electron deficient systems substituents commonly viewed as acceptors may act as donors [23].

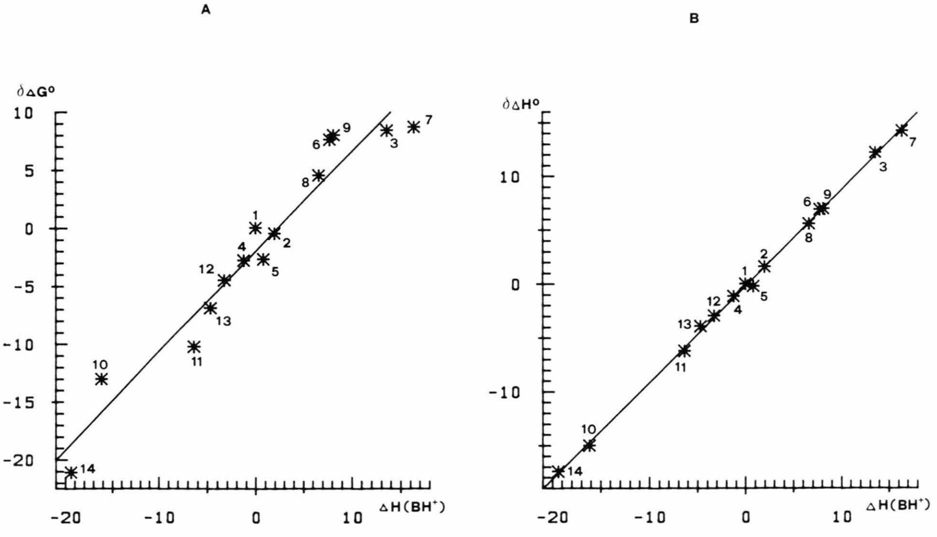


Fig. 1. Correlation of isodesmic stabilization energies $\Delta H\,(\mathrm{BH}^+)$ with experimental relative gas phase basicities $\delta\Delta G^0$ (A) and calculated relative proton affinities $\delta\Delta H^0$ (B) for benzaldehydes.

Alternatively, as an energy rather than a charge based measure of the resonance effect it is tempting to use the difference $\Delta H_R = \Delta H(\mathrm{BH}^+) - \Delta H_{\mathrm{IM}}(\mathrm{BH}^+)$. The validity of converting charge based substituent parameters to energy based ones was already shown in [20] and is confirmed here by the good correlation between $\sum \Delta q_\pi$ and $\Delta H_R$ (benzaldehydes: $r = 0.981$; methylbenzoates: $r = 0.970$). It should be noted, however, that the resonance term defined in this way also contains a contribution from a direct transmission of the field effect ($\pi$-inductive effect) via the phenyl group [20]. As will become evident later this effect, however, seems to be small.

In the spirit of dual substituent parameter treatments, therefore, linear regressions of the form

$$X = a + b * \Delta H_{\mathrm{IM}}(\mathrm{BH}^+) + c * \sum \Delta q_\pi, \qquad (4)$$

$$X = a + b * \Delta H_{\mathrm{IM}}(\mathrm{BH}^+) + c * \Delta H_R, \qquad (5)$$

where $X = \delta\Delta G^0$ or $\delta\Delta H^0$, are employed to describe the effects of substituents. The results of these statistical analyses are collected in Table 3.

Since the coefficients $b$ of (4) are close to unity (Table 3), transmission of the field effect via the phenyl group indeed appears to be small. Furthermore, it has been shown [24] that a quantity which is a linear function of pure variables is also a linear function of composite variables which themselves are linear functions of pure variables. Thus $\Delta H_R$ not only represents a reasonable measure of the resonance effect but also is justified on the basis of the above mentioned composite parameter method [24]. According to [20] a possible refinement (i.e. more exact separation of inductive/field and resonance effects) will consist in defining $\Delta H_R$ by

$$\Delta H_R = \Delta H_R(\mathrm{BH}^+) - b * \Delta H_{\mathrm{IM}}(\mathrm{BH}^+),$$

where the values of $b$ are those obtained by (4). The results for a regression analysis with this definition of $\Delta H_R$ (denoted by 6)) are also listed in Table 3. As can be seen from the data presented there this modification of $\Delta H_R$ does not at all change the quality of the regression analysis. However, in the case of $\delta\Delta G^0$ correlations a significant increase in the relative resonance contribution (measured by the $c/b$ ratio) – especially in the benzaldehyde series – is obtained. It is interesting to compare the relative resonance contributions in the two sets of compounds. The regression analysis for $\delta\Delta G^0$ yields for the ratio $c/b$ (benzaldehydes)/$c/b$ (methylbenzoates) the values 1.44 (4), 1.42 (5), and 1.84 (6), respectively. Thus, the anticipated stabilization by the methoxy group of the positively charged reaction centre leading to a diminished response to substituent resonance effects in the methylbenzoate series [1–4] is clearly reflected in the regression coefficients. Figures 2 and 3 show plots of experimental $\delta\Delta G^0$ and $\delta\Delta H^0$ values obtained by AM1 computations, respectively, versus the corresponding quantities calculated via (5).

Table 2. Results of isolated molecule calculations ($\Delta H_{\mathrm{IM}}$), substituent induced change of $\pi$-electron density, and $\Delta H_R$ (energies in kcal mol$^{-1}$).

| Nr. | Benzaldehydes | | | Methylbenzoates | | |
|---|---|---|---|---|---|---|
| | $\Delta H_{\mathrm{IM}}$ | $\sum \Delta q_\pi$ | $\Delta H_R$ | $\Delta H_{\mathrm{IM}}$ | $\sum \Delta q_\pi$ | $\Delta H_R$ |
| **1** | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **2** | 9.5 | −0.109 | −7.6 | 7.3 | −0.105 | −5.9 |
| **3** | 9.0 | 0.017 | 4.6 | 7.6 | 0.018 | 4.5 |
| **4** | −0.1 | −0.024 | −1.2 | −0.1 | −0.021 | −1.0 |
| **5** | 9.9 | −0.114 | −9.1 | 8.4 | −0.110 | −8.5 |
| **6** | 6.6 | 0.001 | 1.1 | 5.6 | 0.004 | 1.4 |
| **7** | 9.9 | 0.006 | 6.5 | 9.1 | 0.010 | 5.2 |
| **8** | 3.8 | 0.007 | 2.8 | 3.4 | 0.014 | 2.4 |
| **9** | 6.1 | −0.019 | 2.1 | 5.7 | −0.011 | 1.9 |
| **10** | 6.6 | −0.360 | −22.8 | 6.2 | −0.313 | −18.1 |
| **11** | 6.7 | −0.207 | −13.0 | 5.2 | −0.171 | −9.9 |
| **12** | 1.4 | −0.049 | −4.6 | 1.2 | −0.037 | −3.4 |
| **13** | 5.4 | −0.187 | −10.1 | 4.8 | −0.159 | −7.6 |
| **14** | 7.8 | −0.416 | −27.2 | – | – | – |
| **15** | – | – | – | 3.5 | 0.011 | 2.4 |

Table 3. Coefficients ($a$, $b$, $c$) standard error SE, and multiple correlation coefficient $R$ for linear regression equations 4–6 for $\delta\Delta G^0$ (upper values) and $\delta\Delta H^0$ (lower values).

| | Benzaldehydes | | | Methylbenzoates | | |
|---|---|---|---|---|---|---|
| | (4) | (5) | (6) | (4) | (5) | (6) |
| $a$ | 0.017<br>0.404 | −0.372<br>0.020 | −0.373<br>0.019 | −0.092<br>0.147 | −0.266<br>−0.052 | −0.265<br>−0.048 |
| $b$ | 0.810<br>1.075 | 0.598<br>0.859 | 0.433<br>0.927 | 0.935<br>1.069 | 0.727<br>0.833 | 0.679<br>0.891 |
| $c$ | 63.158<br>64.505 | 0.875<br>0.899 | 0.875<br>0.899 | 50.456<br>57.178 | 0.749<br>0.848 | 0.749<br>0.848 |
| SE | 2.578<br>1.868 | 2.096<br>0.302 | 2.096<br>0.303 | 2.042<br>1.386 | 1.633<br>0.230 | 1.631<br>0.228 |
| $R$ | 0.964<br>0.982 | 0.977<br>0.999 | 0.977<br>0.999 | 0.938<br>0.976 | 0.961<br>0.999 | 0.961<br>0.999 |

Quite similar results (cf. Table 3) are obtained by use of (4) and (6). Thus it seems clear that either one of these linear regression treatments is capable to describe substituent effects (including the different response of the two sets of compounds) on the gas phase basicities of the systems investigated in this paper in a completely satisfactory manner.

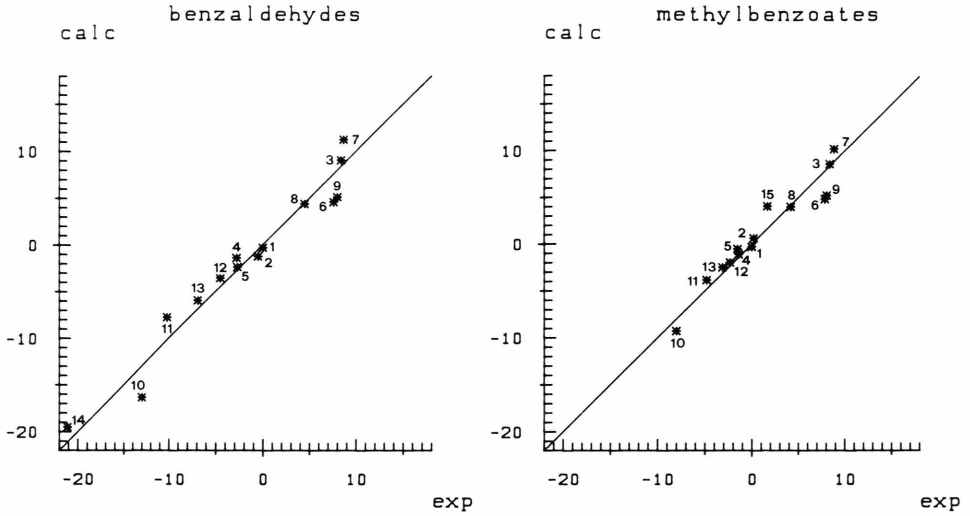


Fig. 2. Plot of experimental relative gas phase basicities (abscissa) versus those calculated via (5) (ordinate).

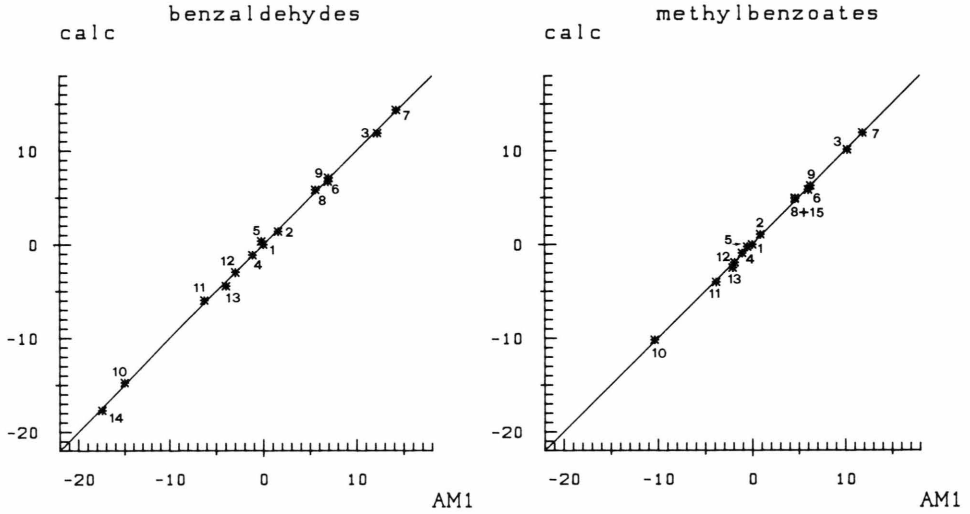


Fig. 3. Plot of calculated relative proton affinities (abscissa) versus those calculated via (5) (ordinate).

[1] M. Mishima, M. Fujio, and Y. Tsuno, Mem. Fac. Sci., Kyushu Univ., Ser. C **14,** 365 (1984).

[2] M. Mishima, M. Fujio, and Y. Tsuno, Mem. Fac. Sci., Kyushu Univ., Ser. C, **15,** 111 (1985).

[3] M. Mishima, M. Fujio, and Y. Tsuno, Tetrahedron Lett. **27,** 939 (1986).

[4] M. Mishima, M. Fujio, and Y. Tsuno, Tetrahedron Lett. **27,** 951 (1986).

[5] J. Bromilow, J. L. M. Abboud, C. B. Lebrilla, R. W. Taft, G. Scorrano, and V. Lucchini, J. Amer. Chem. Soc. **103,** 5448 (1981).

[6] M. Taagepera, K. D. Summerhays, W. J. Hehre, R. D. Topsom, A. Pross, L. Radom, and R. W. Taft, J. Org. Chem. **46,** 891 (1981).

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

[8] J. I. Brauman and L. K. Blair, J. Amer. Chem. Soc. **92,** 5986 (1970); ibid. **93,** 3911 (1971).

[9] M. J. S. Dewar, E. G. Zoebisch, E. F. Healy, and J. J. P. Stewart, J. Amer. Chem. Soc. **107,** 3902 (1985).

[10] M. J. S. Dewar and K. M. Dieter, J. Amer. Chem. Soc. **108,** 8075 (1986).

[11] W. Fabian, Z. Naturforsch. **42a,** 641 (1987).
[12] W. Fabian, J. Comput. Chem., in press.
[13] Y. K. Lau and P. Kebarle, J. Amer. Chem. Soc. **98,** 7452 (1976).
[14] J. F. Wolf, R. H. Staley, I. Koppel, M. Taagepera, R. T. McIver Jr., J. L. Beauchamp, and R. W. Taft, J. Amer. Chem. Soc. **99,** 5417 (1977).
[15] A. Greenberg and J. F. Liebman, J. Org. Chem. **47,** 2084 (1982).
[16] A. Greenberg and T. A. Stevenson, J. Amer. Chem. Soc. **107,** 3488 (1985).
[17] W. J. Hehre, M. Taagepera, R. W. Taft, and R. D. Topsom, J. Amer. Chem. Soc. **103,** 1344 (1981).
[18] R. D. Topsom, J. Amer. Chem. Soc. **103,** 39 (1981).
[19] W. F. Reynolds, P. G. Mezey, and G. K. Hamer, Can. J. Chem. **55,** 522 (1977).
[20] P. G. Mezey and W. F. Reynolds, Can. J. Chem. **55,** 1567 (1977).
[21] R. D. Topsom, Acc. Chem. Res. **16,** 292 (1983).
[22] S. Mariott and R. D. Topsom, J. Mol. Struct. (Theochem.) **106,** 277 (1984).
[23] W. F. Reynolds, P. Dais, R. W. Taft, and R. D. Topsom, Tetrahedron Lett. **22,** 1795 (1981).
[24] M. Charton, A. Greenberg, and T. A. Stevenson, J. Org. Chem. **50,** 2643 (1985).