T echniques for
O rganic
R eactions,
V izualization and
S pectroscopy

P E T R A

Parameter Estimation

for the

Treatment of Reactivity Applications

Version 2.6

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Contents

PETRA is a program package comprising various empirical methods for the calculation of physicochemical properties in organic moleculs.

These methods have been developed over the last 20 years in the research group of J. Gasteiger.

1 Installation

PETRA is available for the following UNIX-derivatives:

- IRIX5.3 up to 6.4
- SOLARIS2.5
- Linux2.0
- HP-UX10.10

in Version 2.6

PETRA comes as a single executable file which has to be stored in the system bin directory or in a user defined directory. In the latter case you have to set the path environment variable accordingly in your .cshrc or .login file. If the file has an extension (e.g., petra.sol) it should be renamed to petra.

2 Usage

PETRA is a command line based program without a graphical user interface.

By default the program looks for a file CTXINP (capitals) which contains the input data. The input file must be written in Gasteiger Cleartext format (CTX). There are several tools available for creating files in CTX format or converting other standard file formats to CTX (see CSED of the CACTVS-Tools, e.g.).

The data required by PETRA are stored under the keywords /MOLECULS, /ATOMS and /BONDS which represent the connectivity table of the considered molecul(s).

In additon, PETRA uses the following keywords:

/HISTORY, /IDENT, /NAME, /STEREO, /VALENCE, /END or /ENDBLOCK

depending on the type of calculations which should be carried out.

The calculated data are written by default into a file called RESULT. This file contains all calculated descriptors in the following manner:

```
 /ATOPROP      1      4
APOLARIZABILITY
[ANGSTROM ** 3]
Effective atom polarizability
R
 /APOLARIZ      3      3
4.4935
5.1220
4.4935
```

Each keyword begins with a slash. PETRA calculates descriptors for properties of ensembles (sets of molecules), molecules, atoms, and bonds. Accordingly the following keywords are provided:

/ENSPROP

/MOLPROP

/BONPROP

/ATOPROP

These keywords indicate what type of property will follow.

After each keyword two integer numbers follow. The first one specifies the number of information units that follow. The second gives the number of lines of the dataset that follows.

In the example shown one information unit with four lines follows after the keyword /ATOPROP. In this case the information unit gives the full name of the property that is following (first line), the physical unit of the data given (second line), an short description of the calculated property (third line) and the number format in which the data are written: R for real number, I for integer number and L for logical (fourth line).

2.1 Synopsis

petra [-option(s)] [inputfile] [outputfile]

If the program is called without any argument it expects the file CTXINP in the working directory and writes the results into a file RESULT.

If one filename is given as argument it will be taken as input file, in case of two, the first is expected to be the input file, the second will be taken as filename for the output data.

2.2 Options

-e[*errorfile*]

    all error messages will be written into the file Petra.err or *errorfile* if given instead of STDOUT.

-l[*logfile*]

    all information about the performed run will be written into the file Petra.log or *logfile* if given instead of STDOUT.

-p[ioc]

Pipe mode selector. This option flags PETRA to be used in a pipe.

    -pi   specifies input pipe mode: petra should read its input file from stdin.

    -po   stands for output pipe mode: petra writes its Cleartext output to stdout.

    -pc   indicates complete pipe mode, combining input and output pipe mode. In output pipe mode petra flushes the buffer after each ensemble.

3 An Overview of the Descriptors Calculated by PETRA

In this section, an overview is given of all descriptors and properties calculated. Each descriptor is to be found in one of the following tables. Table 1 contains all properties calculated for ensemble and molecule properties. Table 2 gives all properties calculated for atoms and table 3 those for bonds.

In Chapter 4 a description of the methods used is given where you can find detailed information on the foundations of the calculation procedures. In the column "Further informations" a shortcut to the respective page is given.

3.1 Properties of Ensembles and Molecules

property/ descriptor	available for a	stored under the keyword	unit	further information
standard heat of formation	Ensemble	/EDELTAHF	kJ/mol	
	Molecule	/DELTAHF	kJ/mol	p.11
molecular polarizability	Ensemble	/EPOLARIZ	$\mathring{A}^3$	
	Molecule	/POLARIZA	$\mathring{A}^3$	p.57
aromatic delocalization energy	Ensemble	/ESTABIL	kJ/mol	
	Molecule	/STABIL	kJ/mol	p.11
ring strain energy	Ensemble	/ESTRAIN	kJ/mol	
	Molecule	/STRAIN	kJ/mol	p.11
number of aromatic atoms	Ensemble	/EAROMAT	-	
	Molecule	/AROMAT	-	-
number of atoms	Ensemble	/ENATOMS	-	
	Molecule	/NATOMS	-	-

number of free electrons	Ensemble	/ENFREEEL	-	
	Molecule	/NFREEEL	-	-
number of π-centers	Ensemble	/EPICENTE	-	
	Molecule	/PICENTER	-	-
number of free electrons	Ensemble	/ERADICAL	No.	
	Molecule	/RADICAL	No.	-
sum of formal positive charges	Ensemble	/EPOSCHAR	electron units	
	Molecule	/POSCHARG	electron units	-
sum of formal negative charges	Ensemble	/ENEGCHAR	electron units	
	Molecule	/NEGCHARG	electron units	-
number of different molecule hash codes	Ensemble	/NHASHMOL	-	ref(1)
number of different atom hash codes	Ensemble	/NHASHATO	-	ref(1)
number of different bond hash codes	Ensemble	/NHASHBON	-	ref(1)
ensemble hash code	Ensemble	/ENSHASH	-	ref(1)
molecule hash code	Molecule	/MOLHASH	-	ref(1)
molecule hash group	Molecule	/MHASHGRP	-	ref(1)

Table 1. All descriptors for ensembles and molecules

ref(1): W.-D. Ihlenfeldt, J. Gasteiger, *J. Comput. Chem*, **8**, 793-813 (1994)

3.2 Bond Properties

property/descriptor	stored under the keyword	unit	further information
bond dissociation energy (BDE)	/BDE	kJ/mol	p.18
total BDE for breaking s/p bonds	/TBDE	kJ/mol	p.18
mean of effective atom polarizability	/BPOLARIZ	Å^3	p.18
difference in π-charge	/DQPI	electron units	p.31
difference in σ-charge	/DQSIG	electron units	p.21
difference in total charge	/DQTOT	electron units	p.39
difference in π-electronegativity	/DENPI	eV	p.31
difference in σ-electronegativity	/DENSIG	eV	p.21
sum of σ-charges shifted across a bond in all iterations	/SQIT	electron units	p.21
resonance stabilization of a positive charge	/PSTAB	-	p.42
resonance stabilization of a negative charge	/NSTAB	-	p.42
resonance stabilization	/STABRES	-	p.42
delocalization stabilization of a positive charge	/PDELOC	eV	p.42

delocalization stabilization of a negative charge	/NDELOC	eV	p.42
delocalization stabilization	/SDELOC	eV	p.42
size of the smallest ring the bond belongs to	/BRINGSIZ	no. of atoms	-
fraction of s-hybridization	/HYBRIDS	-	-
fraction of p-hybridization	/HYBRIDP	-	-
fraction of d-hybridization	/HYBRIDD	-	-
Bond belongs to an aromatic ring	/BAROMATI	FLAG	-
Bond order	/BOORD	-	-
Number of nonhydrogen neighbor atoms	/NONHNEIG	-	-
Bond hash group	/BHASHGRP	-	ref(1)

Table 2. All bond descriptors

ref(1): W.-D. Ihlenfeldt, J. Gasteiger, *J. Comput. Chem*, **8**, 793-813 (1994)

3.3 Atomic Properties

property/descriptor	stored under the keyword	unit	further information
effective atom polarizability	/APOLARIZ	$\mathring{A}^3$	p.57
π-charge	/QPI	electron units	p.31
σ-charge	/QSIG	electron units	p.21
total charge	/QTOT	electron units	p.39
π-electronegativity	/ENPI	eV	p.31
σ-electronegativity	/ENSIG	eV	p.21
lone pair electronegativity	/ENLP	eV	p.31
size of the smallest ring the atom belongs to	/ARINGSIZ	No.	-
atom can form a cation on heterolytic bond cleavage	/B1D0	FLAG	-
atom can form an anion on heterolytic bond cleavage	/B1D2	FLAG	-
atom can be a center for an alpha elimination	/B2D2	FLAG	-
atom can accept another bond	/M1D0	FLAG	-
atom can accept another bond by using two free electrons	/M1D2	FLAG	-
donor atom which can form two new bonds	/M2D2	FLAG	-

atom can accept another bond by using one free electron	/M1D1	FLAG	-
Atom can accept one electron	/B1D1	FLAG	-
Atom belongs to an aromatic ring	/AAROMATI	FLAG	-
Formal charge	/ACHARGE	electron units	-
Atom belongs to a p-system	/APICENTE	FLAG	-
Atomic number	/ATOMICID	No.	-
Number of free electrons	/FREEEL	No.	-
IUPAC group number	/GROUP	No.	-
Number of neighbor atoms	/NEICHBOR	No.	-
Number of nonhydrogen neighbor atoms	/NONHNEIG	No.	-
Atom has one lone electron	/ARADICAL	FLAG	-
Atom hash group	/AHASHGRP	No.	ref(1)

Table 3. All atomic descriptors

ref(1): W.-D. Ihlenfeldt, J. Gasteiger, *J. Comput. Chem*, **8**, 793-813 (1994)

4 Details on the Methods

This section describes the methods the calculations in PETRA are based upon. All methods are empirical in nature and have been developed in the research group of J.Gasteiger et.al.

The following chemical effects can be quantified:
- heats of formation
- bond dissociation energies
- σ-charge distribution
- π-charge distribution
- inductive effect
- resonance effect and delocalization energies
- polarizability effect

4.1 Heats of Formation

The heat of formation ΔH_f^o can be calculated for neutral molecules, radicals, cations, and radical cations in the gas phase at 25 °C.

Heats of formation are estimated from additive contributions of substructures in a molecule.
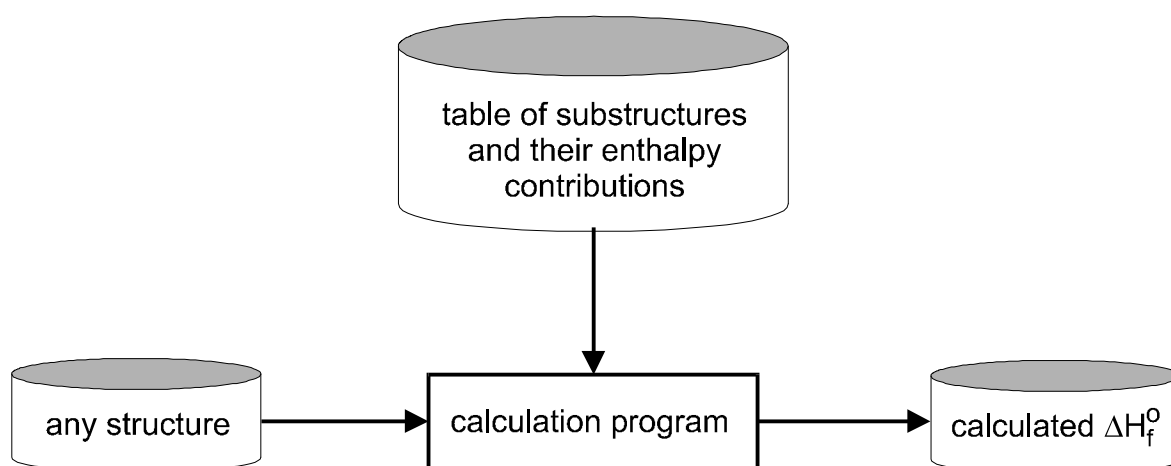
Figure 1. Calculation of ΔH_f^o

The substructures and the values of their contribution to the heat of formation are contained in tables in the program.

The accuracy of an additivity scheme for the estimation of molecular properties is strongly dependent on the number of parameters selected, i.e., on the maximum size of the substructures considered in the approach. With increasing number of parameters the accuracy for reproducing known data increases. However, the predictive power will go down as substructures might be present in structures with unknown properties that have not yet been parameterized. This is actually a trade-off between accuracy and predictive ability. A scheme was chosen that works with

substructures consisting of two, three, or four atoms thus covering the interaction of atoms over one, two, or three bonds (1,2-,1,3-,and 1,4-interactions).

$$A-B \quad A-B-C \quad A-\underset{\overset{|}{D}}{B}-C \quad A-B-C-D$$
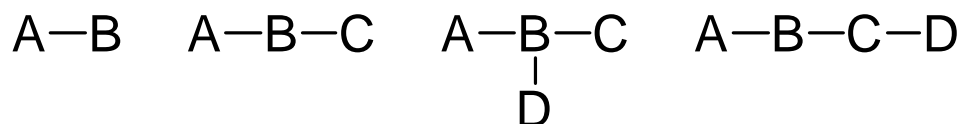
In order to keep the number of parameters within reasonable limits, substructures for 1.4 interactions (A-B-C-D) are taken only, when the central bond is a double bond (B=C).

The numerical value (parameter) for the contribution of a substructure were obtained by a statistical analysis (multilinear regression analysis) of experimental heats of formation. These data are contained in a database that can be updated and the entire scheme can easily be reparameterized when new experimental data have been added to the knowledge base.
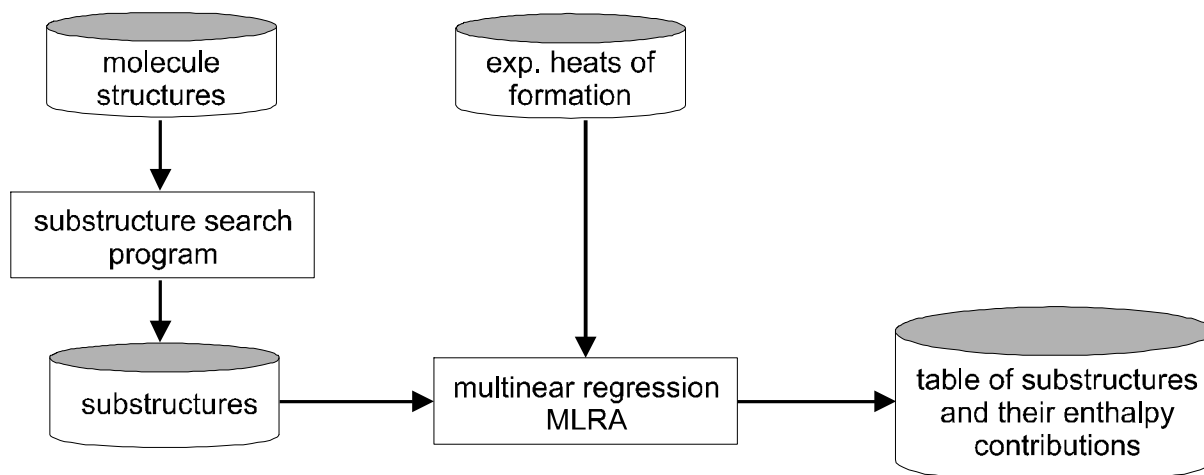

Figure 2. Generation of the knowledge base

Interactions involving hydrogen atoms are only taken for bonds (A-H). For larger substructures they have been set to zero. This is done to allow the determination of parameters by multi-linear regression analysis. Otherwise, the system becomes over-determined and the set of linear equations is linearly dependent and cannot be solved.

Cyclic structures, in particular small rings and aromatic systems, strongly influence heats of formation and therefore additional parameters for strain energies and aromatic delocalization energies must be considered.

For radicals additional atomic parameters for the radical center (A.) have to be determined.
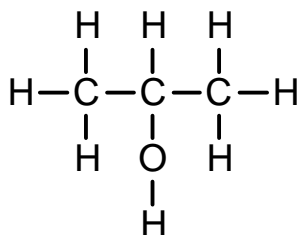
Values calculated

ΔH_f^o **(DELTAHF):**   standard heat of formation

ΔE_{HMO} **(STABIL):** aromatic resonance stabilisation energy

ΔE_{strain} **(STRAIN):** ring strain energy

Example

Calculation of the heat of formation of 2-propanol

No. of occurrences	substructure	contribution in kJ/mol
7	C - H	415,97
2	C - C	332,82
1	O - H	463,48
1	O - C	326,22
1	C - C - C	9,69
2	O - C - C	23,53
1	O - C (- C) - C	-6,28

$$\mathbf{S} = 4417.63 \text{ kJ/mol}$$

Σ of atomization energy of elements = 4146.10 kJ/mol

$$\Delta H_f^o (\text{calc.}) = (4146.10 - 4417.63) \;\; kJ/mol = -271.53 \;\; kJ/mol$$

$$\Delta H_f^o (\text{exp.}) = -272.80 \;\; kJ/mol$$

Results

Some examples for experimental and calculated heats of formation are presented in Table 4.

Compound	composition	ΔH_f^o (exp)	ΔH_f^o (calc)	deviation
2-methylpropane	C_4H_{10}	-134.2	-134.4	-0.2
2-methylpropene	C_4H_8	-16.9	-14.9	2.0
diethylamine	$C_4H_{11}N$	-72.5	-76.7	-4.2
benzene	C_6H_6	82.6	77.2	-5.4
ethanol	C_2H_6O	-235.2	-233.5	1.7
propanoic acid	$C_3H_6O_2$	-453.5	-457.4	3.9
tert-butyl radical	C_4H_9	37.6	37.4	-1.7

Table 4. Examples for calculated and observed heats of formation (all data are given in kJ/mol)

Altogether, approximately 800 organic compounds and 180 radicals have been studied. A short overview of some of the classes of compounds that have been studied, together with the root mean square (RMS) between experimental and calculated heats of formation is given in Table 5.

class of compounds	No. of compounds	RMS
alkanes	61	6.9
alkenes	64	3.8
alcohols	34	11.3
carboxylic acids	26	8.9
esters	36	9.4
ethers	41	8.2
nitro-compounds and amines	87	11.2
halogen compounds	153	6.2
cycloalkanes and aromatic compounds	136	8.1
acyclic carbon hydrogen radicals	32	5.0
hetero atom containing radicals	23	7.5

Table 5.   Classes of organic compounds and root main square errors (RMS in kJ/mol)

Scope and Limitations

Presently, the method has been parameterized for

- neutral molecules
- radicals.

Parameters are available for molecules containing C, H, O, N, S, P, F, Cl, Br, I atoms.

Applications

The enthalpy inherent in a compound is a fundamental factor determining its stability and chemical behaviour. Its experimental determination is tedious and time-consuming. Thus, an estimation scheme is very valuable.

The values of the heats of formation of starting materials (SM) and products (P) of a reaction can be used to calculate the heat of reaction.

$$\Delta H_r = \Sigma \Delta H_f^o (P_i) - \Sigma \Delta H_f^o (SM_i)$$

Thus, the thermochemistry of a process, whether it is exothermic or endothermic, can be determined.

References

1. An Algorithm for Estimating Heats of Reaction
   J. Gasteiger
   Comput. Chem. **2**, 85-88 (1978)
2. Automatic Estimation of Heats of Atomization and Heats of Reaction
   J. Gasteiger
   Tetrahedron **35**, 1419-1426 (1979)
3. Critical Evaluation of Additivity Schemes for Estimating Heats of Atomization
   J. Gasteiger, P. Jacob, U. Strauß
   Tetrahedron **35**, 139-146 (1979)
4. Automatic Estimation of Ring Strain Energies
   J. Gasteiger, O. Dammer
   Tetrahedron **34**, 2939-2945 (1978)

4.2 Bond Dissociation Energies

Bond dissociation energies give the energy necessary for breaking a bond into two radicals (homolytic process).

$$A - B \longrightarrow A\cdot + B\cdot$$
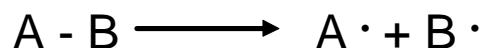
The dissociation energy of a bond, can be calculated from the heats of formation of the molecule and of the two radicals formed by breaking that bond.

$$BDE(A-B) = \Delta H_f^o(A\cdot) + \Delta H_f^o(B\cdot) - \Delta H_f^o(A-B)$$

Heats of formation of the neutral molecule and the two radicals formed by breaking a bond are calculated by the method presented in the previous chapter.

<u>Values calculated</u>

BDE(A-B): bond dissociation energy of a bond between the atoms A and B

if the considered bond is part of a π-system the BDE gives the energy for abolishing the π-interactions. The total amount of breaking that bond (σ- and π-interactions) is given by (see Figure 3)
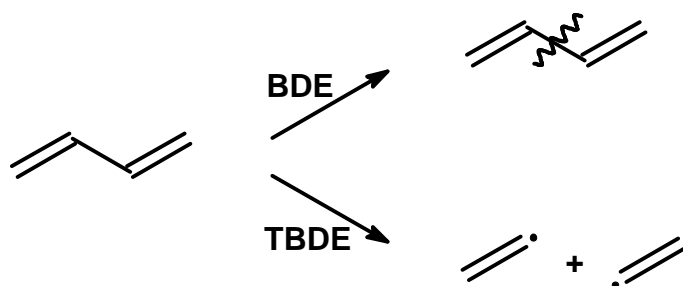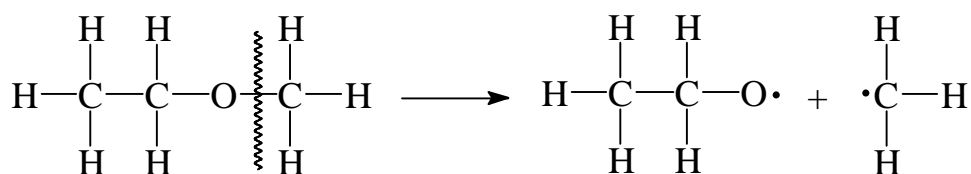
TBDE(A-B): total bond dissociation energy

Figure 3. Difference between BDE and TBDE

Example

The bond dissociation of an ether bond in methylethylether may serve as an example.

ΔH_f^o (exp)   -216.4   -17.2   +143.9

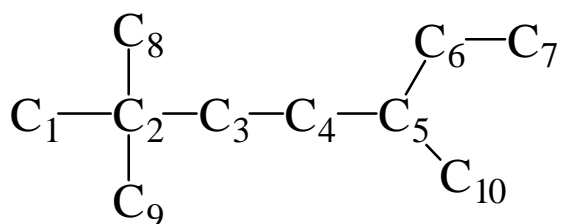ΔH_f^o (calc)   -215.4   -21.0   +142.2

    BDE (exp.) = +343.1 kJ/mol
    BDE (calc.) = (142.2 - 21.0 + 215.4) kJ/mol = +336.6 kJ/mol

Scheme 1. Calculation of the BDE of the Me-O-bond in methylethylether

Results

The example in the following table illustrates that even small changes in the BDE of C-H and C-C bonds can be reproduced.

$$C_1-C_2-C_3-C_4-C_5$$

with C_8 and C_9 on C_2, and C_6-C_7 and C_{10} on C_5

Bond	BDE(calc.)	BDE(exp.)
C_1-H	406.1	410.0
C_3-H	386.6	397.5
C_5-H	379.6	384.9

Bond	BDE(calc.)	BDE(exp.)
C_3-C_4	339.4	342.3
C_4-C_5	337.5	336.4
C_3-C_2	332.3	325.1
C_6-C_7	354.7	354.8
C_5-C_{10}	346.8	352.3
C_1-C_2	341.1	342.3

in kJ/mol

Table 6. Bond dissociation energies of 2,2,5-trimethylheptane

Applications

The bond dissociation energy is a fundamental factor influencing chemical reactivity. It is of paramount importance in radical processes. It has also been shown that the BDE can influence reactivity in polar processes.

Reference

1. Models for the Representation of Knowledge about Chemical Reactions
J. Gasteiger, M. Marsili, M. G. Hutchings, H. Saller, P. Löw, P. Röse, K. Rafeiner
J. Chem. Inf. Comput. Sci **30**, 467-476 (1990).

4.3 *s*-Charge Distribution

The notion of partial charges on the atoms of a molecule is widely used by the chemist. However, it should be kept in mind that this concept is a rather crude reflection of the electron distribution in a molecule and that it has no theoretical foundation. Nevertheless, this model of assigning a non-uniform electron distribution to the individual atoms giving them partial charges has been quite useful.

Partial atomic charges are calculated from orbital electronegativities by consideration of the bond structure (connectivity) of the molecule.

The basis of our approach is the electronegativity concept, electronegativity, χ, as defined by Mulliken as the mean of the ionization potential and the electron affinity:

c = 0.5 (IP + EA)

The various orbitals of an atom are considered separately; each orbital having its own electronegativity value, χ_i. Thus, electronegativity is dependent on the hybridization state of an atom. The initial orbital electronegativity values are those determined by Hinze and Jaffe (references: *J. Am. Chem. Soc.* **84**, 540 (1962); *ibid.* **85**, 148 (1963); *J. Phys. Chem.* **67**, 1501 (1963)).

Electronegativity is not only dependent on the type of orbital being considered but also on its occupation number (n=0,1,2). Electronegativity values can be obtained from the data given by Hinze and Jaffe (see above) for the neutral state (n=1) and for states with a unit positive (n=0) and negative charge (n=2). The occupation of an orbital can be considered as a continous variable, i.e. a continous range of partial charge, q_A, in an atom is allowed. With three values fixed for the dependence of orbital electronegativity on charge (n=0,1,2 corresponding to q = +1, 0, -1), a polynomial of degree 2 can be fitted for the dependence of the electronegativity of an orbital χ_{iA} on the charge, q_A, on an atom.
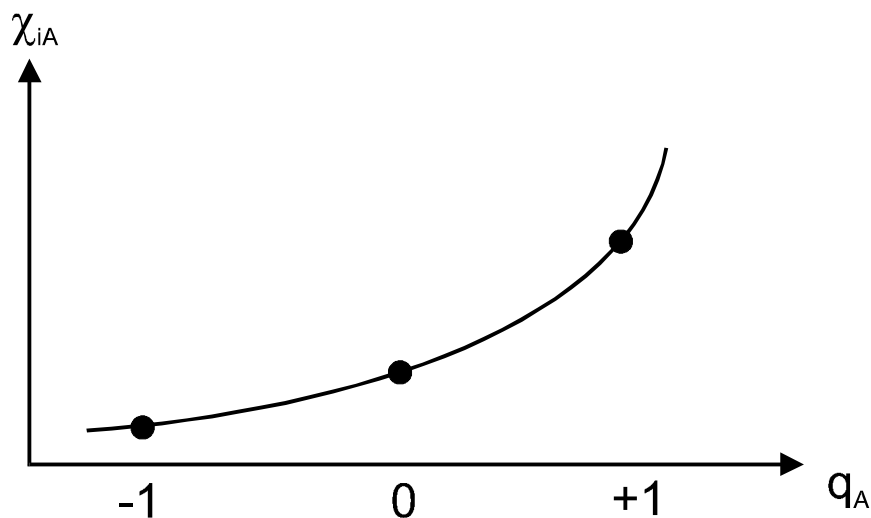
$$c_{iA} = a_i + b_i q_A + c_i q_A^2$$

Figure 4. Dependence of the electronegativity of an orbital i of atom A on the charge q_A

The three values χ_i^+, χ_i^0, χ_i^- allow the determination of the three coefficients, a_i, b_i, c_i, of the dependence of orbital electronegativity on charge.

On bond formation, electron density is transferred from the less electronegative atom, A, to the one, B, with higher electronegativity. This gives atom A a positive charge, thus increasing its electronegativity. Conversely, atom B with higher electronegativity becomes negatively charged, thereby decreasing its electronegativity. In effect, the electronegativities of the atoms bonded together tend to equalize.

But they do so only partially. The electron transfer creates an electrostatic potential that acts against further electron transfer. These ideas form the essence of the method of Partial Equalization of Orbital Electronegativity (PEOE). Partial Equalization of Orbital Electronegativity is realized by an iterative procedure.

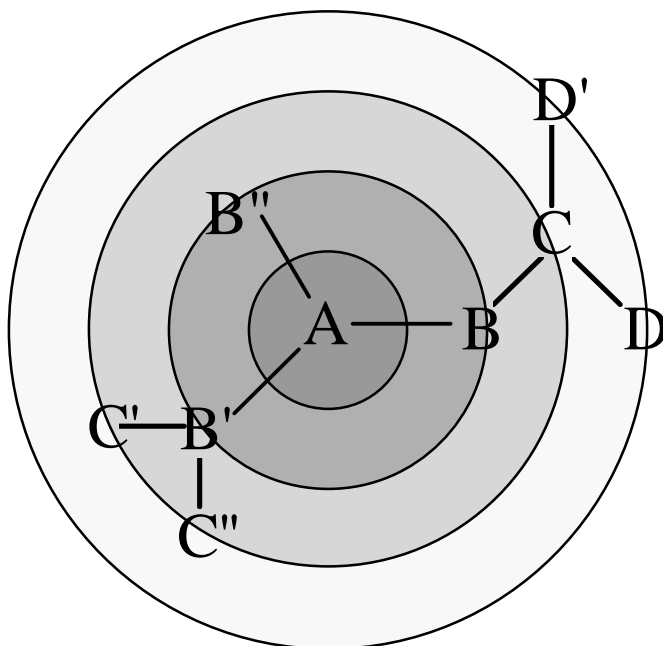This procedure is graphically illustrated by the following figure and scheme.

**Figure 5. Iterative procedure for Partial Equalization of
                Orbital Electronegativity (PEOE)**

Step. 1: for each atom A and orbital i

$$\chi_{iA} = a_i + b_i q_A + c_i q_A^2$$

Step. 2: for each bond A-B

$$\Delta' q_{AB}^{<n>} = (\chi_{iA}^+)^{-1} (\chi_{iA} - \chi_{iB}) * \alpha^n$$

$$\Delta q_{AB} = \Delta q_{AB} + \Delta q_{AB}^{<n>}$$

Step 3.: for all bonds to an atom

$$q_A^{<n>} = \Sigma \Delta q_{AB}^{<n>}$$

$$q_A = q_A + q_A^{<n>}$$

If $n < n_{max}$ go to Step 1

α is a damping factor set to 0.5;

n is the number of the current iteration

Scheme 2. PEOE-Algorithm

The damping mechanism embodied in the factor α^n ensures rapid convergence of the procedure; the number of iterations through the loops is set to 10.

The method has been extended to small ring compounds where sizeable changes in hybridization states occur. In this case, the amount of s- and p-character has to be taken into account in the initial values of the electronegativities (ref. 3).

Values calculated

The following quantities are obtained by the PEOE procedure:

$q_{A,s}$ (QSIG(A)):

At the end, for each atom A of a molecule a unique value for its partial charge, q_A, is obtained.

$c_{A,s}$ (ENSIG(A)):

Due to the dependence of electronegativity on charge, this charge q_A corresponds to a specific value of the electronegativity of this atom, χ_A.

$Dq_{AB,s}$ (DQSIG (AB)):

Difference in the σ-charges on atoms A and B of a bond.

$Dc_{AB,s}$ (DENSIG (AB)):

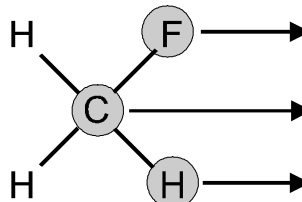Difference in the electronegativities of atoms A and B of a bond.

$Q_{AB,s}$ (SQIT (AB)):

(Sum of charges (Q) shifted in the ITerations)

The amount of charge shifted across a bond, Q^σ, in the course of all iterations is obtained as an additional parameter. It was found that this value can be taken as a measure of the polarity of a bond, being more characteristic than the difference in the total charges on the two atoms of the bond.

Example

The change in the charges during the iterations is illustrated with fluoromethane as an example.

	Start	iterations					q_{end}	χ_{end}
		1	2	3	4	5		
F	0	-175	-218	-237	-246	-251	-253	11.31
C	0	114	91	84	81	79	79	8.72
H	0	20	42	51	55	58	58	7.53
		[milli electronunits]						[eV]

Figure   6.
Fluoromethane as example for the PEOE-procedure

Results

The dissection of the electron distribution in a molecule and its assignment to individual atoms is a drastic oversimplification (where do I have to make the cut in a bond between two atoms?). There is no theoretically sound criterion for the definition of partial atomic charges. Therefore, comparison of the values obtained by our method was made with values calculated by other methods and with physical and chemical data.

A Mulliken population analysis (MPA) is the most widely used quantum mechanical method for the derivation of partial atomic charges. In spite of its known weaknesses (improper handling of the overlap population; heavy dependence on the basis set) it is still very much in use.

For an unambiguous comparison of the results of the PEOE method a set of molecules was chosen for which both theoretical and experimental data were available in the literature. As theoretical data, values on atomic charges from a Mulliken population analysis on STO-3G wave functions were selected. As experimental data C-1s core electron binding energies as obtained from ESCA measurements were chosen for they are known to depend directly on the valence electron distribution.

Table 7 gives a comparison of the PEOE charges with those from the Mulliken population analysis and the C-1s core electron binding energy shifts.

		PEOE	ab initio	C-1s
1	CH_4	-78	-7	0
2	CH_3CH_3	-68	-26	-0.2
3	$CH_2=CH_2$	-106	-156	-0.1
4	HC≡CH	-122	-182	0.4
5	CH_3F	79	169	2.8
6	CH_2F_2	230	383	5.6
7	CHF_3	380	532	8.28
8	CF_4	561	674	11.0
9	$*CH_3CH_2F$	-37	-58	0.2
10	CH_3*CH_2F	87	209	2.4
11	$*CH_3CF_3$	39	-99	1.1
12	CH_3*CF_3	387	546	7.6
13	CH_3OH	33	136	1.6
14	CH_3OCH_3	36	161	1.4
15	H_2CO	115	-167	3.3
16	$*CH_3CHO$	-9	-61	0.6
17	CH_3*CHO	123	211	3.2
18	$*CH_3COCH_3$	-6	-64	0.6
19	CH_3*COCH_3	131	260	3.1
20	HCN	51	-70	2.6
21	$*CH_3CN$	3	62	2.1
22	CH_3*CN	60	21	2.1

Table 7. Partial atomic charges by the PEOE method and a Mulliken population analysis on STO-3G wave functions (all in millielectron-units) as well as C-1s core electron binding energen (in eV).

The PEOE charges show a fairly strong correlation with the MPA charges with a correlation coefficient of 0.939 (ref. 2). The correlation passes through the zero-point and has a slope of 1.31 with the MPA-STO-3G charges having the larger values.

$$q_{MPA} = 1.31 * q_{PEOE}$$

To further explore the quality of the two sets of charge values, a comparison was made with the C-1s core electron binding energy shifts for the same set of compounds. ESCA shifts are those experimental data probably most closely related to the valence electron distribution.

The PEOE charges give a correlation with the ESCA shifts of 0.987 and a standard deviation of 0.27 eV. The Mulliken population analysis charges (STO-3G) show a correlation coefficient of 0.938 and a standard deviation of 0.64 eV. This study showed that the PEOE charges can reproduce the experimental data of C-1s ESCA shifts better than the charges from the Mulliken population analysis on STO-3G wave functions.

More extensive comparisons of the charge values with theoretical and experimental data are reported for total charges after the calculation of π-charges has also been presented (next section).

<u>Scope and Limitations</u>

Presently, the parameters for the initial electronegativity values and their charge dependence have been included for the following types of atoms:

C, H, O, N, B, S (II), P (III), F, Cl, Br, I, Li, Be, Na, Mg, Al, Si, Ti.

<u>Applications</u>

1. Dipole moments have been calculated from the atomic charges for a series of compounds:

Dipole Moments Obtained by Iterative Partial Equilization of Orbital Electronegativity

J. Gasteiger, M. D. Guillen

J. Chem. Research (S) 1983, 304-305; *(M)* 1983, 2611-2624

2. A correlation of the charges on the hydrogen atoms with the ^{1}H-NMR chemical
   shifts was found for a wide variety of organic compounds:

Prediction of Proton Magnetic Resonance Shifts: The Dependence on Hydrogen

Charges obtained by Iterative Partial Equalization of Orbital Electronegativity

J. Gasteiger, M. Marsili

Org. Magn. Resonance **15**, 353-360 (1981)

3. The values of the electronegativities after completion of the PEOE calculations
   (residual electronegativities) are a measure of the inherent power of an atom in
   this specific molecular environment to further attract electron density. In this
   sense, they are a quantitative measure of the inductive effect. This was shown in
   studies of the proton affinities (PA) of alkyl-amines:

Residual Electronegativity - An Empirical Quantification of Polar Influences and its

Application to the Proton Affinity of Amines

M. G. Hutchings, J. Gasteiger

Tetrahedron Lett. **24**, 2541-2544 (1983).

4. The proton affinity data can be calculated by an equation comprising a parameter
   for the polarizability effect (vide infra) and residual electronegativity as a measure
   of the inductive effect.
   Electronegativity values have been used in a variety of multiparameter equations
   quantifying data on chemical reactivity.

These include:

- proton affinities of alcohols and ethers
    as well as

- proton affinities of thiols and thioethers:

See reference:

Quantitative Models of Gas-Phase Proton Transfer Reactions Involving Alcohols,

Ethers, and their Thio Analogs. Correlation Analyses Based on Residual

Electronegativity and Effective Polarizability

J. Gasteiger, M. G. Hutchings

J. Amer. Chem. Soc. **106**, 6489-6495 (1984)

- gas phase acidities of alcohols.

  and

- proton and hydride ion affinities of carbonyl compounds.

See reference:

A Quantitative Description of Fundamental Polar Reaction Types. Proton and Hydride Transfer Reactions Connecting Alcohols and Carbonyl Compounds in the Gas Phase

M. G. Hutchings, J. Gasteiger *J. Chem. Soc. Perkin* **2**, 1986, 447-454

- aqueous phase acidities of alcohols.

  and

- carbonyl hydration equilibria.

See reference:

Correlation Analyses of the Aqueous Phase Acidities of Alcohols and Gem-Diols, and of Carbonyl Hydration Equlibria, using Electronic and Structural Parameters

M. G. Hutchings, J. Gasteiger

J. Chem. Soc. Perkin **2**, 1986, 455-462

References:

1. A New Model for Calculating Atomic Charges in Molecules
   J. Gasteiger, M. Marsili
   Tetrahedron Lett. **34**,3181-3184 (1978)
2. Iterative Partial Equalization of Orbital Electronegativity- A Rapid Access to Atomic Charges
   J. Gasteiger, M. Marsili
   Tetrahedron **36**, 3219-3228 (1980)
3. Extension of the Method of Iterative Partial Equalization of Orbital Electronegativity
   to Small Ring Systems

M. D. Guillen, J. Gasteiger

Tetrahedron **39**, 1331-1335 (1983)

4. Electronegativity Equalization: Application and Parametrization

W. J. Mortier, K. Van Genechten, J. Gasteiger

J. Amer. Chem. Soc. **107**, 829-835 (1985)

5. Electrostatic Interactions in Molecular Mechanics (MM2) Calculations via PEOE Partial Charges. I. Haloalkanes

L. G. Hammarström, T. Liljefors, J. Gasteiger

*J. Comput. Chem.*, **9**, 424-440 (1988)

4.4 π-Charge Distribution

Partial atomic charges in π-systems are calculated by generating all valence bond (resonance) structures for this system and then weighting them on the basis of π-orbital electronegativities and formal considerations (PEPE = Partial Equalization of π-electronegativity).

First the π-system of a molecular structure is determined and those atoms are identified that are starting points of +M or -M effects. The various resonance structures are then generated starting at the acceptor or donor atoms. One or more topological weights are assigned to the various resonance structures that depend on the changes in the valence bond structure and in the formal charges of the atoms at both ends of a resonance structure. These topological weight factors have been optimized from sets of data on ^{13}C NMR shifts of twelve monosubstituted benzene derivatives, ^{13}C NMR shifts of twelve carbon atoms in nine substituted pyridines, and C-1s ESCA shifts of eleven carbon atoms in seven fluorinated olefines.

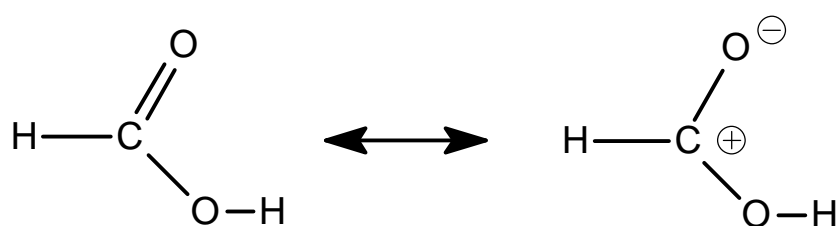- <u>shift of charge</u>

topological weight = 1
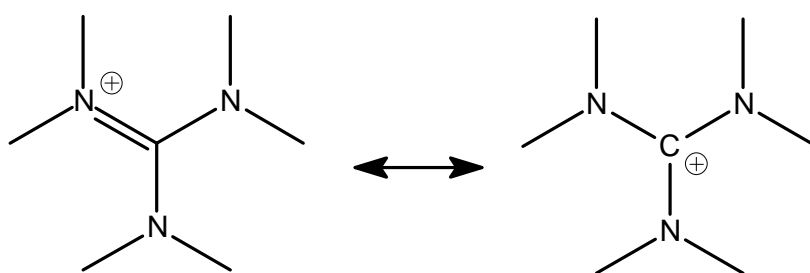
- <u>separation of charge</u>
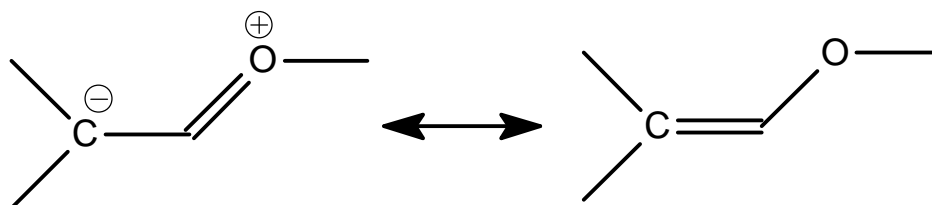
topological weight = 0.5
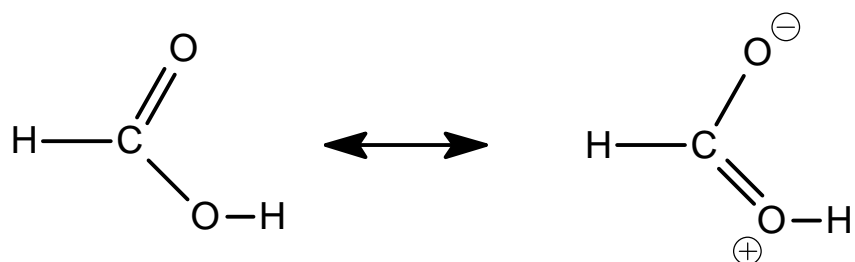
If the positive and the negative charge are on adjacent atoms the topological factor has only a value of 0.25

- <u>recombination of charge</u>

topological weight = 1.0

Scheme 3. Example for the topological weight factor

The total topological weight factor W_t consists of three parts:

$$W_t = f_Q \, f_B \, f_A$$

      f_Q - factor for separation of charge

      f_B - factor, if the number of covalent bonds is decreased

      $f_A = 0.3$ - if an aromatic system is destroyed (e.g. by

              formation of a quinoid system)

In the next step, the resonance structures are weighted based on consideration of their electronic nature. The electronic weight W_e of each resonance structure is derived from π-electronegativities χ_π and the electrostatic influences of neighbouring atoms:

$$W_e = Dc_p + f_e \, Dq_N$$

>$\Delta\chi_\pi$ - difference of the π-electronegativities of those atoms that change its formal charge
>
>$f_e \, \Delta q_N$ - term for the electron repulsion of neighbouring atom

The π-electronegativities are dependent on atom type, hybridisation state and σ-charge. The following equation is applied:

$$c_p = a + b \, q_s + c \, q_s^2$$

Using the product of the topological and the electronic weight the effect of each resonance structure on the charge equalization process is calculated. The charge is moved along the various π-system to the atoms of the resonance structures thereby changing their electronegativity. Therefore, the process of weighting the structures and shifting electron density has to be repeated in several cycles with decreasing amounts of charge being shifted.

Values calculated

The following quantities are obtained by the PEPE procedure:
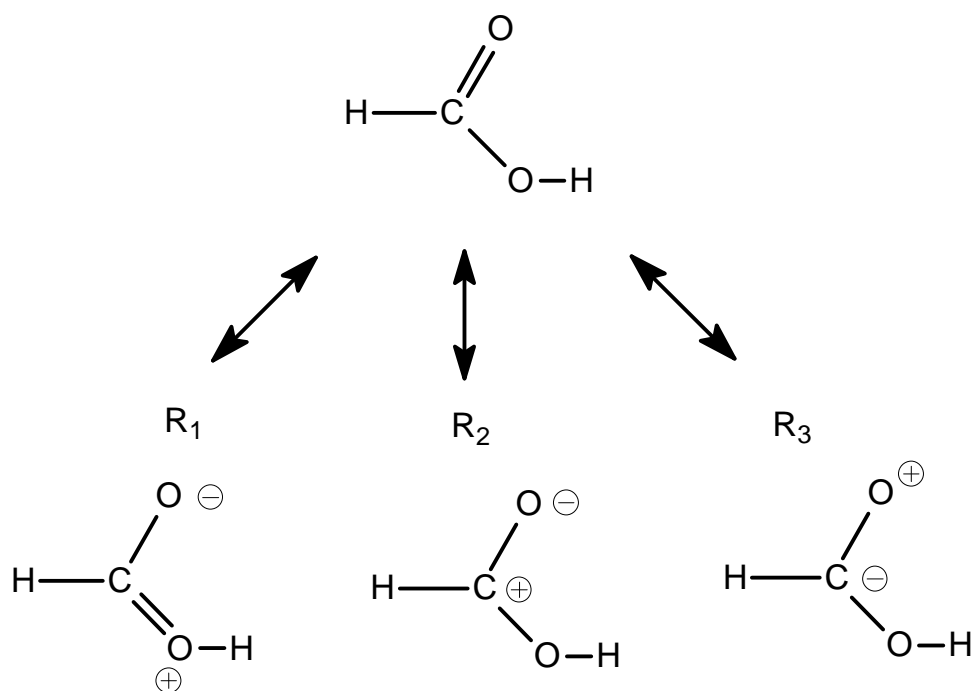
$q_{p,A}$ (QPI (A)):   π-charge on atom A

$c_{p,A}$ (ENPI (A)):   π-electronegativity of atom A

$Dq_{p,AB}$ (DQPI (AB)):   Difference on the π-charges on atoms A and B

Dc_p,AB (ENPI (A)):   Difference in the π-electronegativities of atoms A and B of a
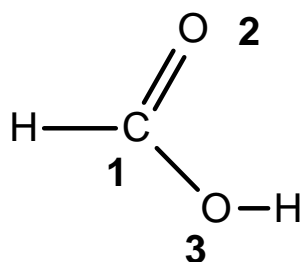   bond

c_LP,A (ENLP (A)):   Lone pair electronegativity of atom A

Example

	charge separation	charge separation of atoms bonded directly decrease of the number of covalent bonds	charge separation of atoms bonded directly decrease of the number of covalent bonds
w_t	**0.5**	**0.1625**	**0.1625**

Scheme 4. Determination of topological weights

Changes of p-charges:

atom number	1	2	3	
χ_π	6.690	8.568	3.747	Cycle 1
q_π	-0.01	-0.004	0.005	
χ_π	6.720	8.290	3.977	Cycle 2
q_π	0.003	-0.026	0.022	
χ_π	6.895	7.301	4.802	Cycle 8
q_π	0.022	-0.119	0.097	

Contribution of the various resonance structures:

	$R_1: 2 \neg 1 \neg 3$	$R_1: 1 ® 2$	$R_1: 2 ® 1$	
charge shifted	-0.005	0.001	-0.001	cycle 1
	-0.017	-0.005	0.005	cycle 2
	-0.016	-0.004	0.004	cycle 3
	-0.014	-0.004	0.004	cycle 4
	-0.010	-0.002	0.002	cycle 8

Scheme 5. Process of charge equalization including electronic weighting

Results

The π-charges calculated by the PEPE method for various heterocycles containing nitrogen atoms were compared with values from a Mulliken population analysis of ab initio STO-3G wave functions.

• pyridine derivatives:

Pyridine and 2- and 4-hydroxy pyridine derivatives show similar π-charge patterns. The nitrogen and the carbon atoms at the 3- and 5- position have negative charges in the range of 0 and -0.125 e and the atoms at the 2-,4- and 6- position have positive charges in the range of 0 and +0.125. The results of the STO-3G and the PEPE-calculations correspond with each other to a reasonable degree.
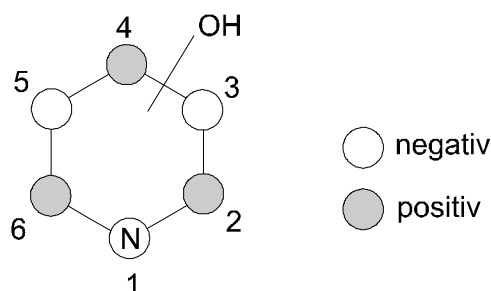

R	N_1	C_2	C_3	C_4	C_5	C_6	O	
H	-0.13	0.07	-0.03	0.06	-0.03	0.07	-	*ab initio*
	-0.08	**0.02**	**0.00**	**0.04**	**0.00**	**0.02**	**-**	**PEPE**
2-OH	0.13	0.06	-0.09	0.07	-0.08	0.04	0.131	*ab initio*
	-0.11	**0.02**	**-0.01**	**0.05**	**-0.01**	**0.02**	**0.051**	**PEPE**
3-OH	-0.01	-0.09	0.03	-0.03	0.02	-0.05	0.115	*ab initio*
	-0.08	**0.00**	**0.00**	**0.02**	**0.00**	**0.01**	**0.044**	**PEPE**
4-OH	-0.07	0.04	-0.12	0.07	-0.08	0.04	0.125	*ab initio*
	-0.10	**0.02**	**-0.01**	**0.03**	**-0.01**	**0.02**	**0.057**	**PEPE**

Table 8.   Comparison of π-charges in pyridine derivatives calculated by PETRA and STO-3G, respectively (ab initio values from: J. E. Del Bene, *J. Comp. Chem.* **2**, 251-260 (1981))

- pyrimidine derivates

PEOE π-charges of pyrimidines, which are substituted at the 4-position, a show well agreement with the corresponding values from a Mulliken population analysis of STO-3G wave functions (see next page):
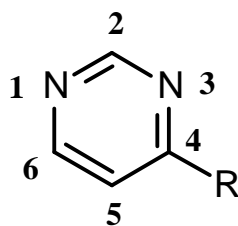
R	N$_1$	C$_2$	N$_3$	C$_4$	C$_5$	C$_6$	
H	-0.04	0.01	-0.04	0.03	0.01	0.03	*ab initio*
	-0.08	**0.04**	**-0.08**	**0.06**	**0.00**	**0.06**	**PEPE**
Me	-0.06	0.03	-0.07	0.07	-0.02	0.04	*ab initio*
	-0.08	**0.04**	**-0.08**	**0.06**	**0.00**	**0.06**	**PEPE**
NH$_2$	-0.12	0.05	-0.15	0.09	-0.09	0.06	*ab initio*
	-0.11	**0.04**	**-0.12**	**0.06**	**-0.03**	**0.06**	**PEPE**
OH	-0.09	0.05	-0.14	0.06	-0.05	0.06	*ab initio*
	-0.10	**0.04**	**-0.11**	**0.05**	**-0.01**	**0.06**	**PEPE**
F	-0.07	0.04	-0.10	0.03	-0.04	0.06	*ab initio*
	-0.09	**0.04**	**-0.11**	**0.05**	**-0.01**	**0.06**	**PEPE**
CH=CH$_2$	-0.16	0.03	-0.07	0.05	-0.01	0.04	*ab initio*
	-0.09	**0.04**	**-0.10**	**0.06**	**0.00**	**0.06**	**PEPE**
CHO	-0.04	0.02	-0.05	0.03	0.02	0.04	*ab initio*
	-0.07	**0.04**	**-0.08**	**-0.05**	**0.02**	**0.06**	**PEPE**
CN	-0.03	0.03	-0.04	-0.01	0.03	0.05	*ab initio*
	-0.07	**0.04**	**-0.08**	**0.04**	**0.01**	**0.07**	**PEPE**

Table 9   Comparison of p-charges in pyrimidine derivatives calculated by PETRA and STO-3G, respectively (ab initio values from: J. E. Del Bene, *J. Comp. Chem.* **2**, 251-260 (1981))

Scope and Limitations

The dependence of the π-electronegativity on charge is parameterized for the following atoms.

- π_z- electronegativity: Be, B, C, N, O, Al, P, S
- lone pair electronegativity: C, N, O, F, P, S, Cl, Br, J

(The functions are dependent on the hybridization states)

Applications

A detailed discussion will be given in the next section using the results of the calculations on both the σ- and π-charges.

References

1. Pi-Charge Distributions from Molecular Topology and Pi-Orbital Electronegativity
   M. Marsili, J. Gasteiger
   Croat. Chem. Acta **53**, 601-614 (1980)
2. Berechnung der Ladungsverteilung in konjugierten Systemen durch eine Quantifizierung des Mesomeriekonzeptes
   Gasteiger, H. Saller
   Angew. Chem. **97**, 699-701 (1985)
   Angew. Chem. Intern. Ed. Engl. **24**, 687-689 (1985)

4.5 Total Charges

Total charges are obtained by summation of the results of the calculations on σ- and π-charges (see the two preceding sections).

<u>Values calculated</u>

$q_{A,tot}$ (QTOT (A)):   Total charge on atom A

$Dq_{AB,tot}$ (DQTOT (AB)):   Difference in the total charges on atoms A and B of a bond

Some systematic investigations have been made to compare the PEOE total charges with those from Mulliken population analyses (MPA). Because of the strong dependence of MPA on the basis set, only MPA values from the same basis set should be compared. The choice fell on a MPA of ab initio STO-3G wave functions as this basis set is known to give reasonable partial charges. Furthermore, a large variety of results is available in the literature. Altogether, STO-3G charge values were found in the literature for 63 compounds. This dataset was augmented with calculations on another 65 molecules performed for the purpose of this comparison. It is known that ab initio STO-3G calculations tend to overestimate the polarization of bonds. Therefore, comparison was made not with atomic charges but with group charges, obtained by adding the charges of terminal atoms to that of the atom to which they are bonded. Table 10 summarizes the results obtained for neutral species.

class of compounds	no. of cpds	no. of groups	correlation coefficient
hydrocarbons	9	31	0.82
halogen cpds	23	74	0.83
nitrogen cpds	19	55	0.76
oxygen cpds	16	56	0.97
boron cpds	9	31	0.98
phosphorous (III)-cpds	4	13	-0.92
sulphur (II)cpds	9	25	-0.18

Table 10. Comparison of PEOE charges with values from a Mulliken population analysis on *ab initio* (STO-3G) group charges

The hydrocarbons cover only a small range of charge values. Therefore small changes in the charge values strongly influence the correlation. In fact, deleting the point for methane that has the largest deviation, improves the correlation coefficient to 0.92.

The results for the nitrogen compounds are somehow disappointing. The largest derivations occur for compounds having nitrogen-oxygen bonds (nitrile oxides, oxaziridine etc.). Apparently, the separation of the electron density in an N-O bond is handled differently by the two methods.

The results of the oxygen and boron containing compounds show an extremely good agreement.

For the phosphorous-III and sulphur-II compounds (thiols, thioaldehyds, thioacids) no correspondence in the charge values was found. In fact, the charge values of the PEOE method run against those from the MPA. No decision can be made whether this is a deficiency of the PEOE or of the MPA charges.

Application

Several physical properties have been correlated or calculated from the charge values. Dipole moments can be calculated from the total charges when the atomic

coordinates are available. 3D-coordinates can be obtained from the CORINA system. The following set of three compounds shows that the effect of through-conjugation in p-nitroaniline is taken into account by the procedure calculating π-charges.
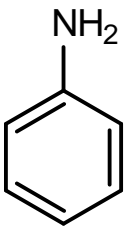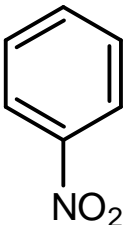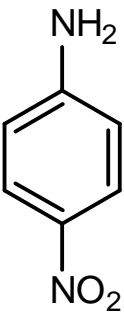
	NH_2 (structure)	NO_2 (structure)	NH_2 / NO_2 (structure)	
Experimental	1.15	4.16	6.91	[Debye]
Calculated	0.90	4.29	6.87	[Debye]

Table 11. Predicting dipole moments for compounds with p-systems

(using σ- and π-charges; automatic 3D structure generation by CORINA with computed bond length correction for the aromatic system)

4.6 Resonance Effect

The stabilization of the positive and the negative charge obtained in the polar breaking of a bond is calculated from the π- and lone pair-electronegativity values of the atoms that are in conjugation to the atoms obtaining the charges.

The search for the atoms that can stabilize a positive or a negative charge does not start at the atoms of the bond that is broken. Rather, the search is initiated the other way round, starting at the atoms that have the potential of stabilizing charges through the resonance effects (source atoms). Then, the atoms of those bonds are marked that will be in conjugation to the source atoms.
The following types of source atoms are considered:

- donor atoms (bearing a free electron pair)
- acceptor atoms (being able to accept an electron pair)
- alkyl groups at multiple bonds (hyperconjugation effect)
- alkyl groups at donor atoms (hyperconjugation effect).

Resonance stabilization is a bond property since it is a bond that is being broken to generate charges. As there are two directions for breaking a bond in a polar manner, each bond is investigated twice:

$$A-B \longrightarrow B^+ + :A^-$$
$$A-B \longrightarrow A^+ + :B^-$$
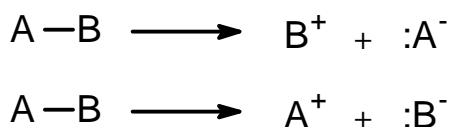
A bond is characterized by the indices of the two atoms A, B comprising the bond. The convention is that the first atom obtains the positive charge.
A value, R^-, is calculated for stabilizing the negative charge and another value, R^+, for stabilizing the positive charge. Furthermore, both values are combined into an additional value, $R^\pm$, for resonance stabilization of the charges at both atom centers. See Figure 7 for details.
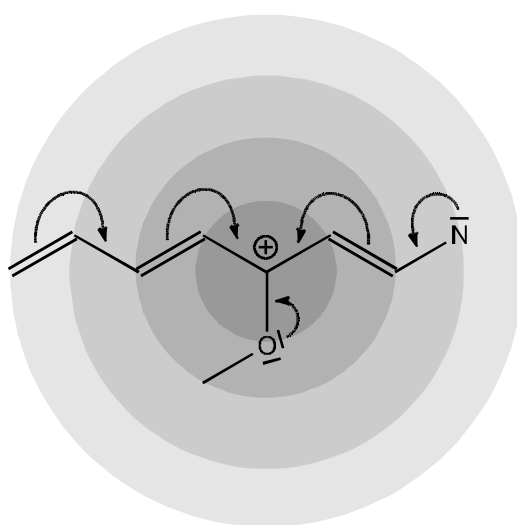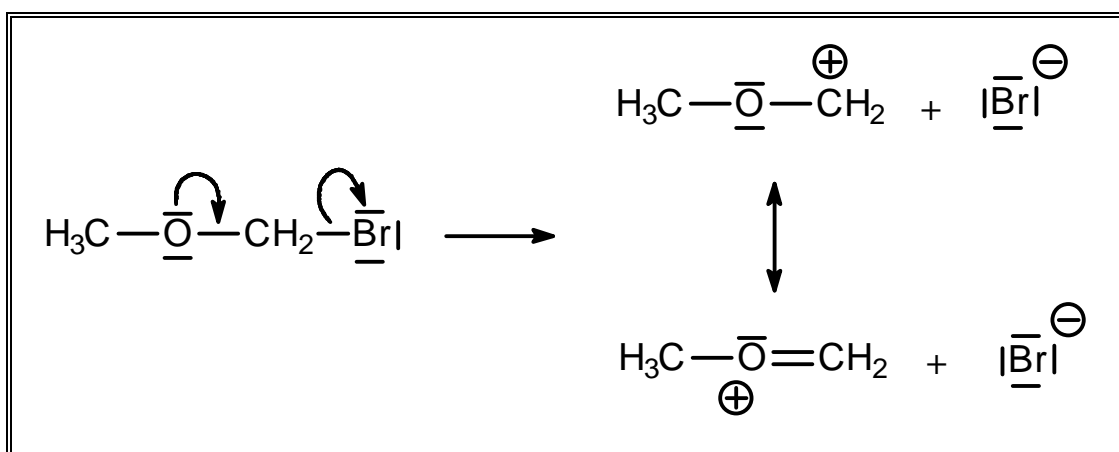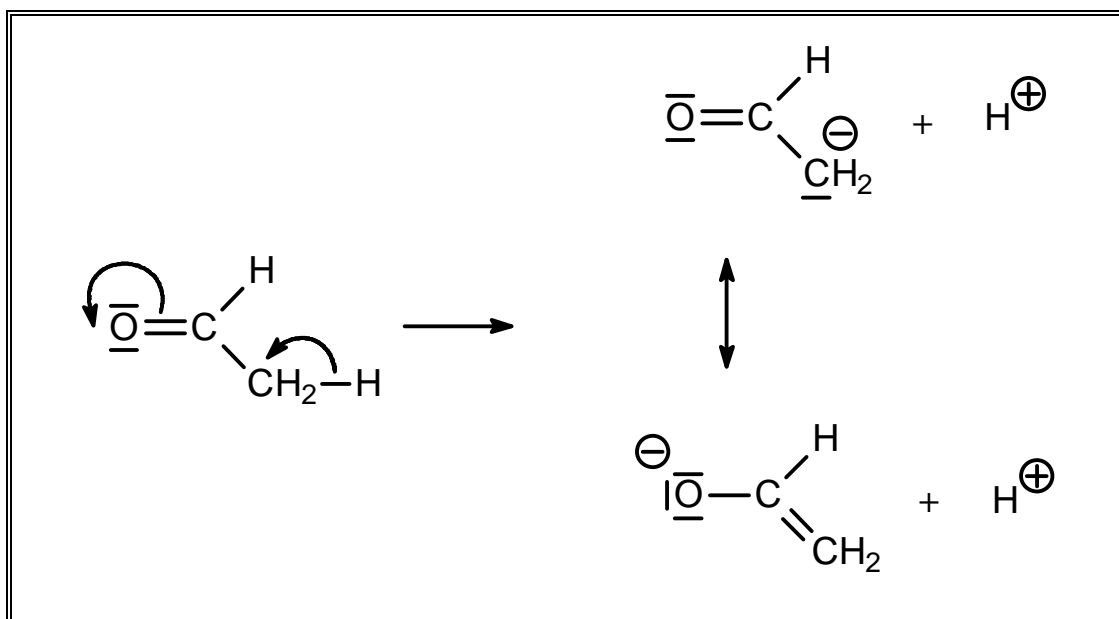
Figure 7. The generation of resonance structures on breaking a bond

The numerical value for the stabilization of a negative charge, R^-, is obtained from all those atoms, i, that will stand in resonance to the negative center:

$$R^-(A-B) = \sum_i f^n c_{p,i}$$

The summation goes over all atoms, i, of the resonance structures. The parameter f is a fading factor which is set to 1.0 if the intervening bonds are aromatic, otherwise f = 0,67. The variable n is the number of bonds between the negative center and the atom, i, (source atom) that, can take over this negative charge in a resonance structure.

The value for the stabilization of the positive charge, R^+, is obtained by the following equation:

$$R^+(A-B) = \frac{c}{\sum_i f^n c_{p,i}}$$

Again, the summation runs over all atoms, i, of the various resonance structures, f is the fading factor having the same values as above, and n is the topological distance between the positive center and the atom, i, that can take over the positive charge.

The constant, c, was set to a value of 26.63 eV under the assumption that a CC-double bond can stabilize a positive or a negative charge at an adjacent CH_2-group to the same extent. In other words, allyl resonance in the cation and in the anion is assumed to have the same stabilizing effect.

The value of the combined effect, $R^{+/-}$, is obtained simply by adding R^+ and R^- of the inverse bond.

$$R^{+/-} = R^+(A-B) + R^-(B-A)$$

Values Calculated

R^+_{AB} (PSTAB (A,B)):

Extent of resonance stabilization of a positive charge on A when the bond A-B is broken in a polar manner.

R⁻$_{AB}$ (NSTAB (A,B)):

Amount of resonance stabilization of a negative charge on A when the bond A-B is heterolytically broken

R⁺ᐟ⁻$_{AB}$ (STABRES (A,B)):

Amount of resonance stabilization of a positive charge on A and a negative charge on B.

<u>Results</u>

The parameter on resonance stabilization is empirical in nature. To establish its importance comparison has to be made with physical or chemical data. No property has yet been found that is directly related to this concept of resonance stabilization. However, the values calculated for resonance stabilization have been very useful in many multi-parameter correlation (see applications).

<u>Applications</u>

The parameter for resonance stabilization has been found to be extremely useful in many applications. Particularly, when studying data on chemical reactivity, this parameter is quite often the singly most important influence. However, as already mentioned, nearly all applications found so far involve multi-parameter equations.

Ionization potentials are data that should, and have indeed been found to give useful applications for the parameter on resonance stabilization of positive charges. Since, on ionization, a positive charge is generated in a molecule and must somehow be accommodated. Any effect contributing to a stabilization of this positive charge should lower the value of the ionization potential.

In fact, it was found that the values for ionization from lone pair or π-orbitals over the entire range of organic compounds could be reproduced well if these compounds are ordered into five different classes:

- aromatic compounds
- carbonyl compounds

- olefines and acetylenes
- olefines and acetylenes with heterodynes in conjugation
- compounds with unconjugated lone pair electrons (heteroatoms).

For each one of these five classes multiparameter equations have been developed, each one of the first four involving the parameter, R^+, for resonance stabilization of a positive charge. Here, the study on ionization potentials of alkenes is presented in more detail to develop an understanding of how the resonance parameter can be used.
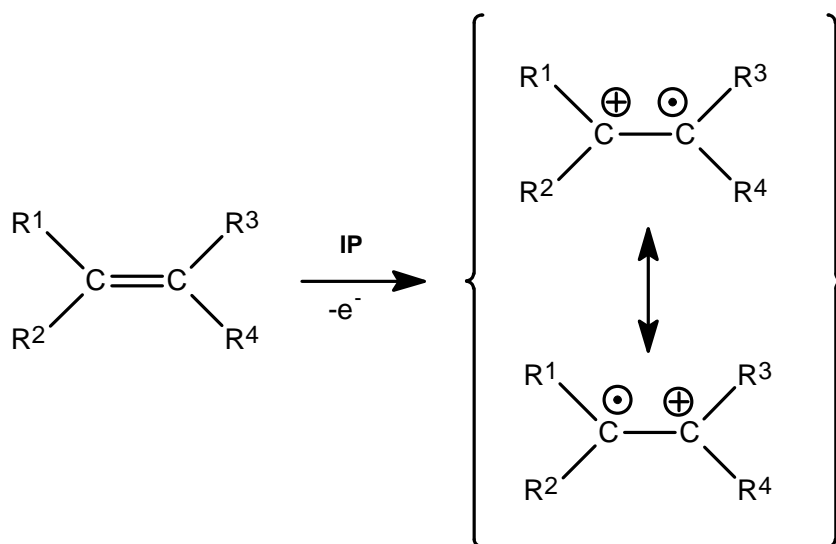
Ionization from the highest occupied molecular orbital (HOMO) of an olefin leads to a radical cation that can be described by two resonance structures. Thus, this ionization is formally quite similar to the process that is used for the definition of the parameter for resonance stabilization:
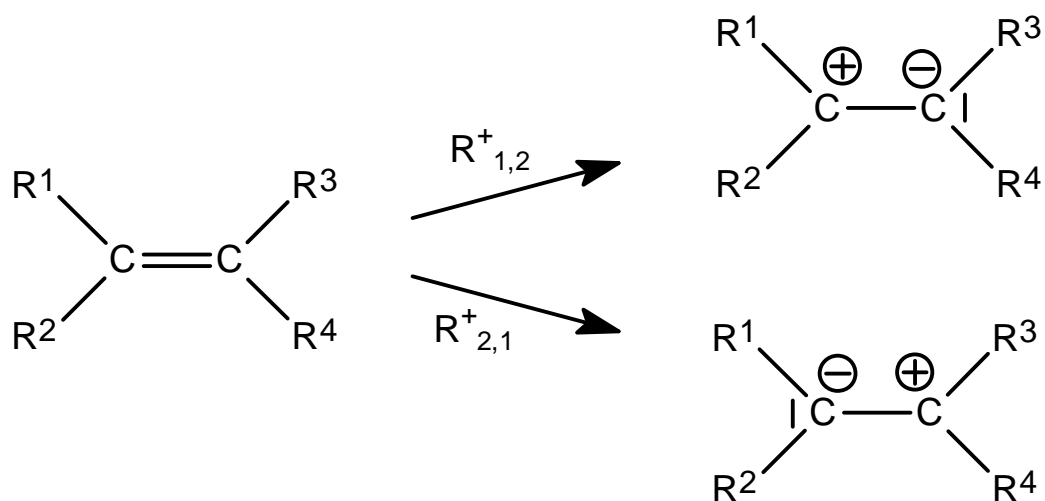
(Remember, the first index of an atom pair specifies that atom of a bond that receives the positive charge).

The fact that two resonance structures are necessary for describing the ionized HOMO indicates that both resonance parameters $R^+_{1,2}$ and $R^+_{2,1}$ should be used for reproducing the ionization potential. In fact, we used the average, $\overline{R^+}$, of these two parameters as a measure of stabilization of the positive charge in the HOMO by resonance (or, to be the more exactly here: hyperconjugation, as only alkylsubstituted alkenes were investigated).

$$\overline{R^+} = 0.5 \; (R^+_{1,2} + R^+_{2,1})$$

In addition to this stabilization mechanism, the stabilization of a positive charge by the polarizability effect (vide infra), as expressed by the parameter α_b for the double bond, had to be used. The final equation obtained by multilinear regression analysis of the ionization potential of 56 alkenes was:

(1) $IP = 10.88(\pm 0.09) - 0.14(\pm 0.01)\overline{R^+} - 0.19(\pm 0.02)a_b$

This equation can reproduce the ionization potentials of these compounds with a standard deviation of 0.11 eV (regression coefficient, r = 0.980).
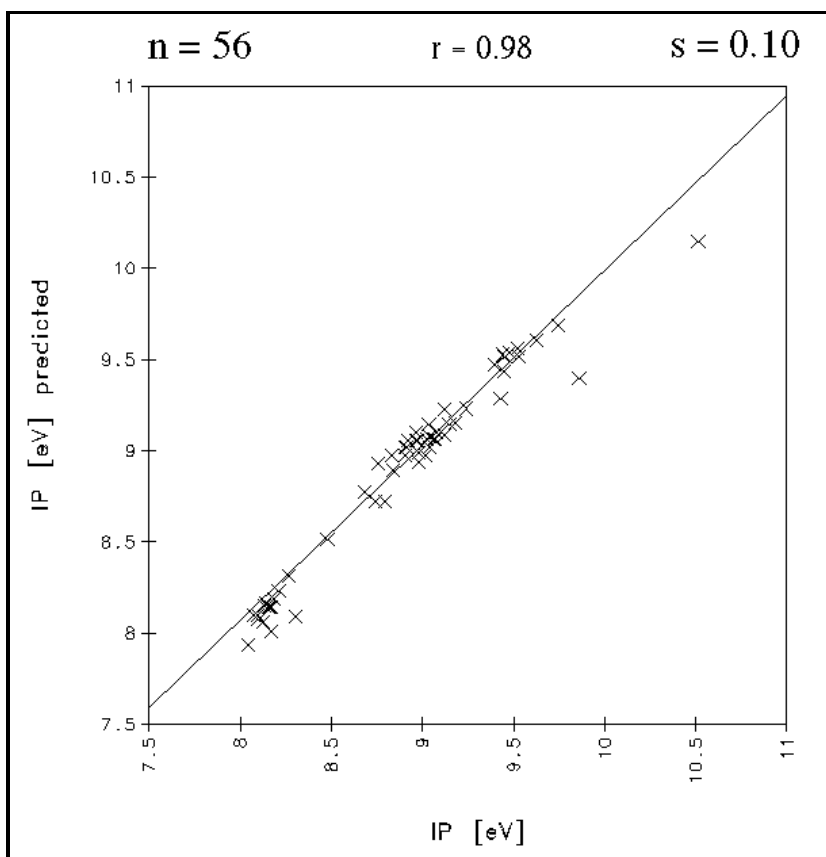
Figure 8. Calculation of Ionization Potentials of alkenes by equation 1

The largest deviations are found for ethylene itself as the first member of the series, and for strained alkenes, cyclopropene e. g.

Parameters for resonance stabilization of charges produced on polar breaking of bonds have been found useful in many studies of data on chemical reactivity. In these cases it is always useful to write down explicitly the mechanism of a reaction. This allows one to deduce the correct resonance parameter that should be used.

For example, the rate determining step of the hydrolysis of amides under basic conditions is:
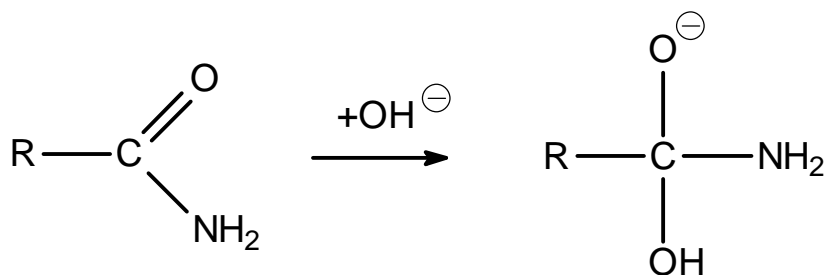
Thus, the CO-double bond is broken in the rate determining step, suggesting that the following resonance parameter should be used:
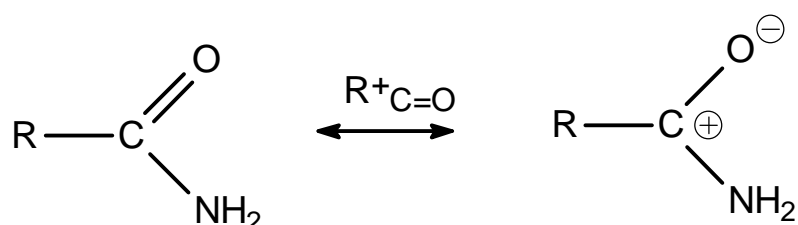
In fact, this parameter was found to be of good modelling power for the calculation of rate data on hydrolysis of amides under basic catalysis.

<u>Reference</u>

H. Saller, *Dissertation*, TU München, 1985

The resonance variables R^+, R^-, $R^{+/-}$ have be shown to be powerful in estimating the resonance stabilization. Nevertheless, it has to be beared in mind that there is no real physical foundation of them. Since the calculation of R^+ bases on the reziprocal values of the π-electonegativity resulting in the unit [1/eV] while R^- is given in [eV] all three descriptors have another unit although they have the same physical meaning. Furthermore, in fact, the energy of resonance stabilization in allylic cations and anions is not equal and this assumption means to be a simplification.

Thus, another variable has been developed for quantifying the delocalization of charges. Analogues to the resonance variable they are called delocalization variables D^+, D^- and $D^{+/-}$.

$D^{+/-}$ gives the mesomeric stabilization of the positive and negative charge in the fragments resulting from a heterolytic bond cleavage.

$$D\pm(b) = D^+ + D^-$$
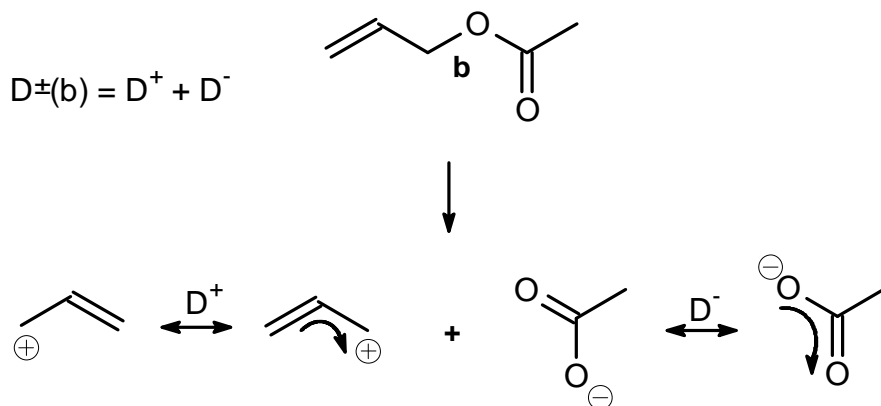
$D^{+/-}$ is depending on the direction in which the bond is broken:

$$D^\pm(A \rightarrow B) = D^+(A^+, A \rightarrow B) + D^-(B^-, A \rightarrow B)$$

$A \rightarrow B$ - bond to be broken in heterolytic manner

For calculating $D^+(A^+, A \rightarrow B)$ and $D^-(B^-, A \rightarrow B)$ the following equations are applied:

$$D^+(A^+, A \rightarrow B) = \left(c_p(A, q_p) - \frac{\sum_{i=1}^{n} c_p(c_i)}{n} \right) \cdot s_p^+$$

$$s_p^+ = \sum_{i=0}^{n} f_j \cdot m$$

f_j - donor potential of the atom or bond typ j

m - number of the atom or bond typ j

$$D^-(B^-, A \rightarrow B) = -\left(c_p(B, q_p) - \frac{\sum_{i=1}^{n} c_p(c_i)}{n} \right) \cdot s_p^-$$

$$s_p^- = \sum_{i=0}^{n} g_j \cdot k$$

g_j - acceptor potential of the atom or bond typ j

k - number of the atom or bond typ j

$c_p(A, q_p')$ - π-electronegativity of the charge center A with the charge q_p'

$c_p(X_i)$ - residual π-electronegativity of source of stabilization X_i

s_p^+ / s_p^- - donor and acceptor potential of the π-system

The stabilization of the charges on the fragments is predicted from charge distribution of the compound in the ground state before breaking the bond. The π-electronegativity serves as a measure for the delocalization potential of the atoms being part of the π-system and is obtained by the PEPE-procedure (see 4.4)

The π-electronegativity of the charge centre is calculated by distributing the formal charge one moiety in the σ-system the other in the π-system. This leads to updated total charges which are used in calculating χ_π by the known polynomial of degree 2:

1a. $q_{\boldsymbol{p}}^{'}(A) = q_{\boldsymbol{p}}(A) + 0.5$ 　　　1b. $q_{\boldsymbol{s}}^{'}(A) = q_{\boldsymbol{s}}(A) + 0.5$

2. $q_t = q_{\boldsymbol{p}}^{'} + 0.5 \; q_{\boldsymbol{s}}^{'}$

3. $c_{\boldsymbol{p}} = a \; q_t^2 + b \; q_t + c$

The factors $s_{\boldsymbol{p}}^{+}$ and $s_{\boldsymbol{p}}^{-}$ give the total donor/acceptor potential of the bond and atom typs of the π-system in the considered structures.

The bond and atom parameters f_j and g_j are standardized to the C-C double bond which is set arbitrary to 1.

f_j was derived from 219 different substituted allylic compounds by considering the proton affinities calculated by AM1:

Bond	$f_j/f(C{=}C)$		Atom	$f_j/f(C{=}C)$
aro	0.5		NR$_2$	2.6
C=C	1.0		OR	2.3
C=O	0.4		SR	1.7
C=S	0.4		PR$_2$	0.5
C=N	0.6		F	0.9
N=C	1.4		Cl	0.6
C≡C	1.0		Br	0.1
C≡N	0.6		J	-0.2
N≡C	1.4		Me-X	0.6
			Me-X=X	0.7

Table 12. Atom and bond parameters for calculating D^{+}

For the determination of g_j a dataset of 37 gas phase acidities was taken:

bond	$g_j/g(C=C)$
aro	0.6
C=C	1.0
C=O	2.2
S=O	1.2
N=O	3.0
C≡N	2.9

Table 13. Atom and bond parameter for calculating D^-

In addition, two exeptional cases have to be considered:

for the stabilization of an aromatic or an antiaromatic system which was formed by a heterolytic bond cleavage the factors s_p^+ and s_p^- must be modified by addition of a further factor $f_{aro}=g_{aro}=2$ in case of aromaticity or substruction in case of antiaromaticity, respectively.

If an atom changes its hybridisation state to sp the f and g parameters are fixed to $f_{vic}=g_{vic}=0.5$ due to the formation of an orthogonal π-system.

Values calculated:

$D^+{}_{AB}$(PDELOC(A-B)):

Extent of delocalization stabilization of a positive charge on A when the bond A-B is broken in a polar manner.

$D^-{}_{AB}$(NDELOC(A-B)):

Extent of delocalization stabilization of a negative charge on A when the bond A-B is broken in a polar manner.

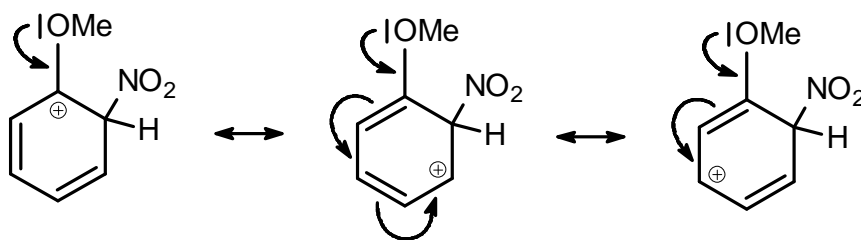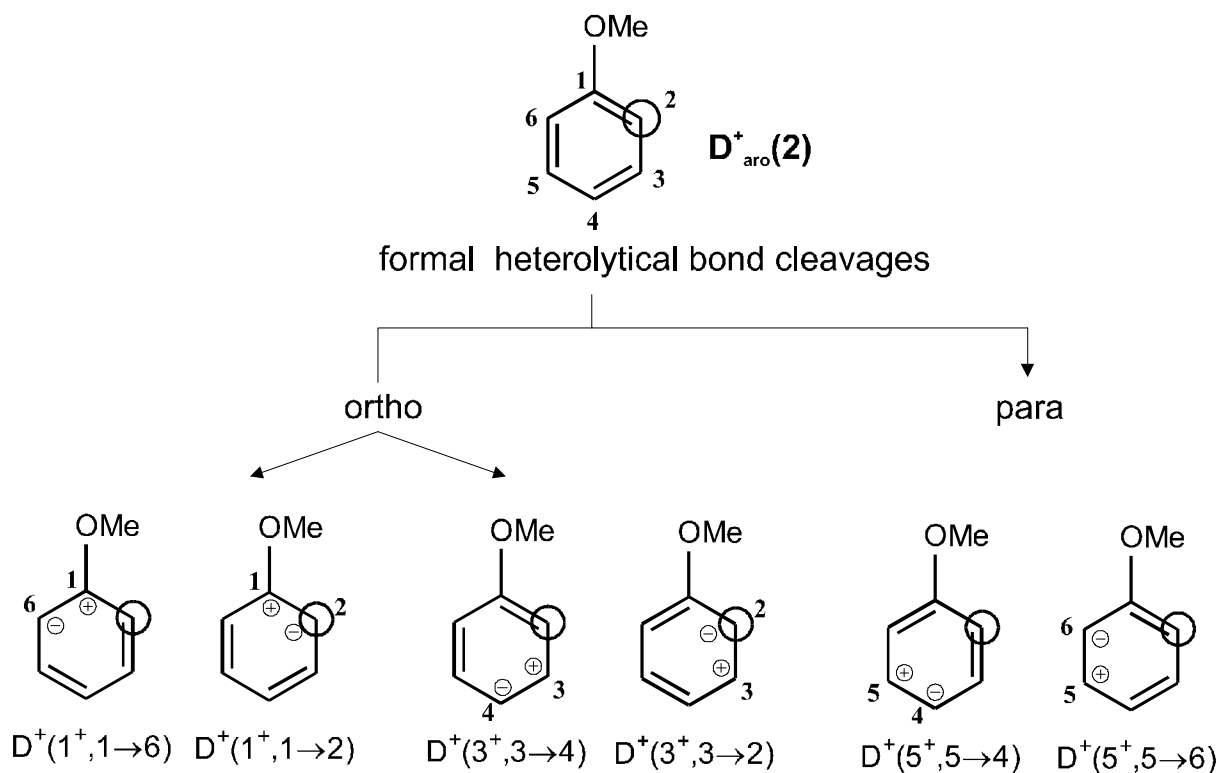**$D^-{}_{AB}$(NDELOC(A-B)):**

Amount of delocalization stabilization of a positive charge on A and a negative charge on B.

Example:

As example should serve the electrophilic aromatic substitution of mono substituted benzene derivatives. It is well known that π donor groups activate the ortho and para position while the meta position is activated by π acceptors.

This fact should be quantified by the delocalization variable D^+.

For calculating D^+ all formal bond cleavages of aromatic π-bonds have to be considered which are resulting in a positive charge in ortho or para position of the reaction centre. By summing up all D^+ parameters for every broken bond $D^+_{aro,position}$ could be obtained:

Stabilization of the positive charge in the σ-complex

Prediction from the ground state

$$D^+_{aro}(2)$$

formal heterolytical bond cleavages

ortho   para

$D^+(1^+,1{\rightarrow}6)$ $D^+(1^+,1{\rightarrow}2)$ $D^+(3^+,3{\rightarrow}4)$ $D^+(3^+,3{\rightarrow}2)$ $D^+(5^+,5{\rightarrow}4)$ $D^+(5^+,5{\rightarrow}6)$

$$D^+_{aro}(2) = D^+(1^+,1 \rightarrow 6) + D^+(1^+,1 \rightarrow 2) + D^+(3^+,3 \rightarrow 4) + D^+(3^+,3 \rightarrow 2) + D^+(5^+,5 \rightarrow 4) + D^+(5^+,5 \rightarrow 6)$$

Figure 9. Determination of the delocalization variable D^+_{aro} in the s-complex

Table 14 shows the calculated values for some mono substituated benzene derivatives compared to benzene.

The different donor potential of the different subtituents can be cleary seen.

compound	$D_{aro}^+(2)$	$D_{aro}^+(3)$	$D_{aro}^+(4)$
benzene	38.0	38.0	38.0
nitrobenzene	36.9	46.2	36.9
methoxybenzene	95.3	38.7	95.3
chlorobenzene	48.4	38.2	48.4

Table 14. D_{aro}^+ of ortho, meta and para position of some selected benzene derivatives

Reference

Angela Fröhlich, *Dissertation*, TU München, 1993

4.7 Polarizability Effect

Polarizability values are calculated from additive increments typical of an atom in a specific hybridization state. When values for the effect of polarizability on charge stabilization are calculated these increments are considered only to an extent that reflects the number of bonds between the atom considered and the charge or reaction center.

It is important to note that these two publications give the procedure that was originally developed by modification of a method for the estimation of the sum of atomic static polarizability (α) as given by K. J. Miller and J. A. Savchik (*J. Am. Chem. Soc.* **101**, 7206 (1979)). The presently used procedure is no longer the one referenced in the above two publications but is a modification of a method for the estimation of the sum of atomic static polarizability as published by Y. K. Kang and M. S. Jhon (*Theor. Chim. Acta* **61**, 41 (1982)). The results of the new method are for the most part similar to those of the originally published one. However, the new approach removes a deficiency of the old method that atoms with many electrons (Cl, S) far away from the reaction center unduly lowered the values for effective polarizability.

Mean molecular polarizability (MMP), α_{mol}, can be estimated from additive contributions, α_i, of atoms as shown by Kang and Jhon (see above). The values of those atomic increments are different depending on the hybridization state of the atoms.

$$\overline{a}_{mol} = \sum_{i}^{atoms} \overline{a}_i$$

The stabilization of charge in a molecule due to polarizability rapidly decreases with distance from the charge center. This decrease is described by a simple damping model, which uses the contribution of each atom, α_i, in a molecule only to an extent that accounts for the number of bonds, n_{ij}, between the charge center, j, and the atom, i.

$$\boldsymbol{a}_{jd} = \sum_i^{atoms} 0.5^{n_{ij}} \boldsymbol{a}_i$$

It should be noted that the value of the effective polarizability, α_{jd}, is thus a property of the atom being considered as the charge or reaction center. This is illustrated in the next figure for the nitrogen as the center of protonation.
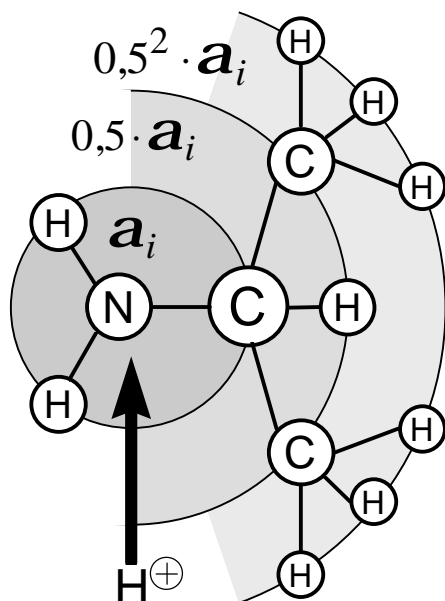

Figure 10. Evaluation of the effective polarizability of N as center of protonation

The value of effective polarizability, α_{jd}, must be seen as a quantitative measure of the stabilization energy resulting from the effect of polarizability.

The bond polarizability, α_b, is calculated as the mean value of the polarizabilities of the two atoms of a bond.

Values calculated

a_{mol}(POLARIZA):   mean molecular polarizability

a_{jd}(APOLARIZ(A)): effective atom polarizability

a$_b$(BPOLARIZ(AB)): bond polarizability, which is the mean value of the

polarizabililies of the atoms A and B

Example

The site dependence of the values for the effective polarizability α_{jd} can be seen with the example of N,N-dimethyl ethylenediamine. The value at the tertiary nitrogen atom, α_{1d}, is with 6.93 Å^3 much larger than the one at the primary nitrogen atom with, α_{2d}, 4.73 Å^3, reflecting the increased tendency of the former atom to accept a positive charge on protonation.
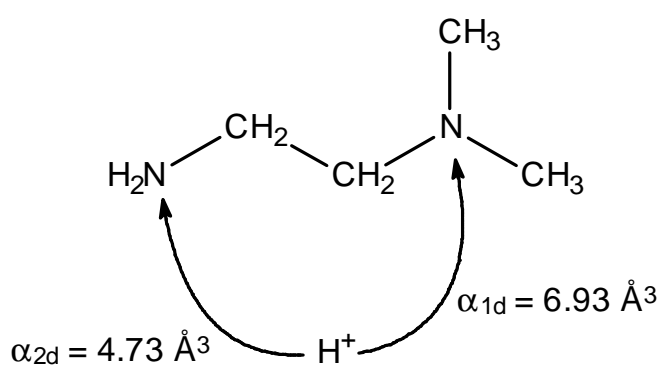

Figure 11. Site dependence of a$_d$

Results

Only values for the mean molecular polarization are given as they can directly be compared with experimental data.

Molecule	PETRA	Kang, Jhon
water	1.43	1.44
diethyl ether	8.78	8.78
diethyl ketone	9.96	9.96
acetic acid	5.11	5.12
acetamide	5.93	5.92
triethylamine	13.27	13.27

Table 15. Mean molecular polarizabilities [Å^3]

Y. K. Kang, M. S. Jhon, *Theor. Chim. Acta* **61**, 41 (1982)

Scope and Limitations

Presently, the following atoms and hybridization states have been parameterized:

H, C_{sp3}, C_{sp2}, C_{sp}, N_{sp3}, N_{sp2}, O_{sp3}, O_{sp2}, P_{sp3}, S_{sp3}, S_{sp2}, F, Cl, Br, I.
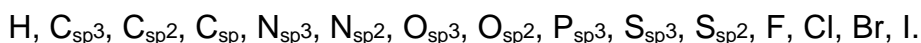
Parameters of aromatic and fused aromatic carbon atoms are not included in the program.

Applications

The use of mean molecular polarizability can be found in textbooks on physical chemistry and will not be further discussed here.

Rather, we want to demonstrate the usefulness of the damping model and the values of effective polarizability calculated with it. Effective polarizability is a parameter that has found many uses in investigations of data on chemical reactivity. However, to get a clear picture of the significance of effective polarizability values we were searching for physical data that were solely dependent on such values. We found such data in combinations of ESCA and Auger spectroscopy.

Through ESCA experiments shifts in the core electron binding energies of chlorine atoms in different molecules may be determined. Auger spectroscopy deals with an additional ionization (KLL spectra) and can be used to determine shifts in Auger kinetic energy.

$$RCl \xrightarrow[-e^-]{ESCA} RCl^+ \xrightarrow[-e^-]{Auger} RCl^{++}$$

The shifts in core-ionization energy and in the Auger kinetic energy make it possible to determine relaxation energies that were shown to be directly related to the polarizability of the ligands of the ionized atom (E. J. Aitken, M. K. Banl, K. D. Bomben, J. K. Gimzewski, G. S. Nolan, T. D. Thomas, *J. Am. Chem. Soc.* **102**, 4873 (1980)). We could show that these relaxation energies correlate directly with the effective polarizability values on chlorine calculated for 13 different organochlorine compounds (r = 0.958; std. dev. 0.10 eV) (ref. 2).

If values on mean molecular polarizability, α, are used, the correlation is much worse (r = 0.885; std. dev. 0.21 eV), showing the superior modelling power of the damping procedure.

Similarly good results were obtained for measurements of such ESCA/Auger relaxation energies in organo germanium compounds (ref. 2).

The largest benefits of the values of effective polarizability have been obtained in studies of data on chemical reactivity. A series of data on gas phase reactions has been investigated as these reactions show the reactivity of individual molecules uncorrupted by solvent effects. Furthermore, data of high quality have become available through high pressure mass spectrometry and ion cyclotron resonance measurements.

Protonation of amines in the gas phase is exothermic, the energy released is called proton affinity (PA).

Polarizability is thought to be a primary source for stabilization of such ions produced in the gas phase.
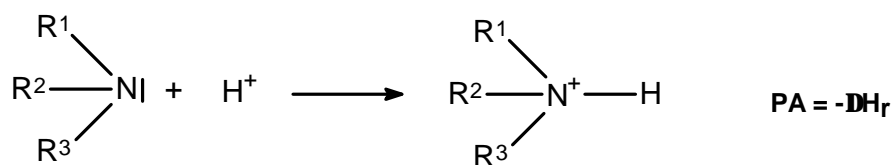
In fact, it can be shown that the proton affinity of unsubstituted alkyl amines can be reproduced by an equation having effective polarizability as the only parameter (ref. 2).
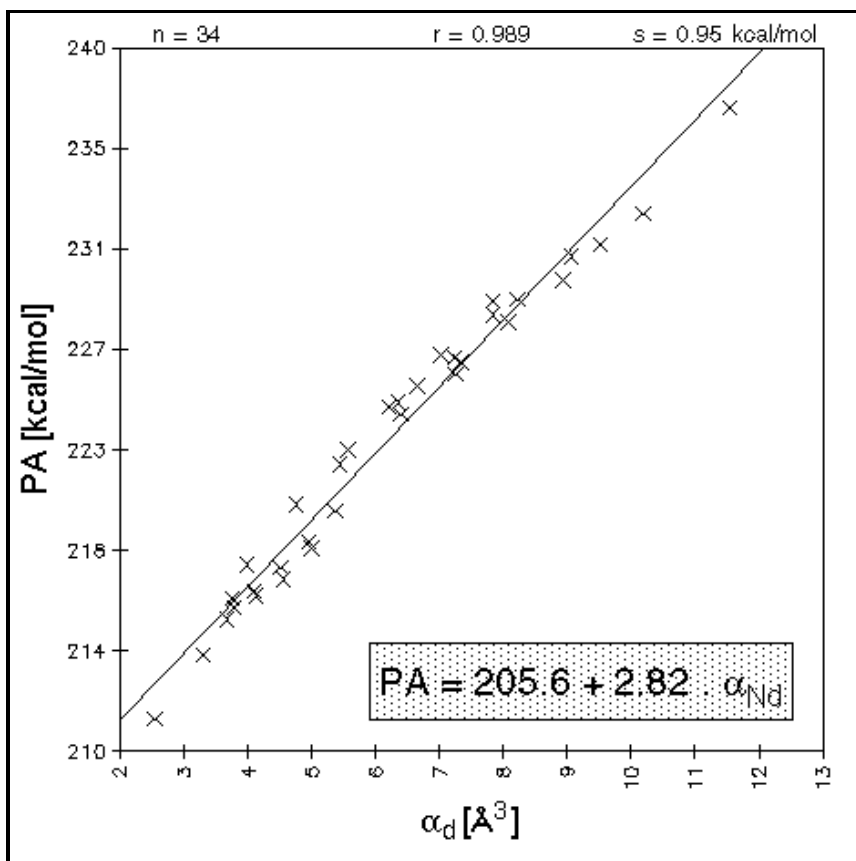
Figure 12. Proton affinity of alkyl amines

The data set consisted of 34 primary, secondary, and tertiary amines of different skeletal type.

If substituents are introduced into the alkylamines, the inductive effect of these heteroatoms has to be accounted for. This was accomplished by introducing, in addition to the values of effective polarizability, an electronegativitiy parameter, χ_s. The resulting two parameter equation reproduced well the proton affinity of 80 unsubstituted and substituted alkylamines (ref. 1).

(2) $PA(kJ/mol) = 1435.5 - 116.3\chi_s + 12.5\alpha_{Nd}$

Such multiparameter equations could be derived for a series of fundamental polar gas phase reactions. The next table gives a summary of these investigations indicating which parameters were found to be necessary for a quantitative description of the data. Effective polarizability values were needed in all cases underlining the importance of this effect, at least in the gas phase.

Reaction	parameters				comment
	α_d	χ	hyp.	ref.	
$\geq$NI + H$^+$	x			1	unsubst. only
$\geq$NI + H$^+$	x	x		2	80 subst. amines
$\geq$OI + H$^+$	x	x		3	ether,alcohols
$\geq$SI + H$^+$	x	x		3	thiols, thioethers
$-$O$-$H $\cdot$ H$^+$	x	x		4	acidity of alcohols,
$\geq$C$=$O + H$^+$	x	x	x	4	
$\geq$C$=$O + H$^-$	x	x	x	4	aldehydes,
$\geq$C$=$O$^+$$-$H + H$^-$	x	x	x	4	ketones

Table 16. Parameters used in linear equations of type (2) for calculating data on gas phase reactions

α_d = effective polarizability

χ = electronegativity parameter for inductive effect

hyp.: parameter for hyperconjugation

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