

CHAPTER-2

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METHODOLOGY

The whole work is based on computational chemistry; hence the computational tools and related definitions and procedures are described below under different captions.

Description of Software Used for Evaluation of Parameters: -

MOPAC

MOPAC is a general-purpose semiempirical molecular orbital package for the study of solid state and molecular structures and reactions.

The semiempirical Hamiltonians MNDO^[1], MINDO/3^[2], AM1^[3], PM3^[4], and MNDO-d^[5-6] are used in the electronic part of the calculation to obtain molecular orbitals, the heat of formation and its derivative with respect to molecular geometry. Using these results MOPAC calculates the vibrational spectra, thermodynamic quantities, isotopic substitution effects and force constants for molecules, radicals, ions, and polymers. For studying chemical reactions, a transition state location routine^[7] and two transition state optimizing routines^[8-9] are available. For users to get the most out of the program, they must understand how the program works, how to enter data, how to interpret the results, and what to do when things go wrong.

While MOPAC calls upon many concepts in quantum theory and thermodynamics and uses some fairly advanced mathematics, the user need not be familiar with these specialized topics. MOPAC is written with the non-theoretician in mind. The input data are kept as simple as possible, so users can give their attention to the chemistry involved and not concern themselves with quantum and thermodynamic exotica.

The simplest description of how MOPAC works is that the user creates a data-file, which describes a molecular system and specifies what kind of calculations and output are desired. The user then commands MOPAC to carry out the calculation using that data-file. Finally the user extracts the desired output on the system from the output files created by MOPAC. The name MOPAC should be understood to mean "Molecular Orbital Package". The origin of the name is somewhat unusual, and might be of general interest: The original program was written in Austin, Texas. One of the roads in Austin is unusual in that the Missouri-Pacific railway runs down the middle of the road. Since this railway was called the MO-PAC, when names for the program were being considered, MO-PAC was an obvious contender.

Most of the theory used in MOPAC is in the literature, so that in principle one could read and understand the algorithm. However, it is convenient to have the theory gathered together in one document. The theory given here is intended for users who (a) want to modify MOPAC, or (b) want to understand how MOPAC does what it does. All derivations can be followed with a little patience, and, as far as possible, "It can be shown that" jumps in logic have been avoided.

There are five distinct methods available within MOPAC: MINDO/3, MNDO, AM1, PM3, and MNDO-d. All are semiempirical, and have roughly the same structure. A complete knowledge of these methods is not necessary in order to use MOPAC; however, a superficial understanding of these methods and their relationship to *ab initio* methods is important for using MOPAC and particularly for interpreting the results.

The five methods within MOPAC have many features in common. They are all self-consistent field (SCF) methods, they take into account electrostatic repulsion and exchange stabilization, and, in them, all calculated integrals are evaluated by approximate means. Further, they all use a restricted basis set of one s orbital and three p orbitals (p_x , p_y , and p_z) per atom (except MNDO-d, which has five d orbitals in addition to the s .p basis set) and ignore overlap integrals in the secular equation. Thus, instead of solving

$$|H - ES| = 0,$$

the expression

$$|H - E| = 0,$$

in which H is the secular determinant, S is the overlap matrix, and E is the set of eigenvalues, is solved. These approximations considerably simplify quantum mechanical calculations on systems of chemical interest. As a result, larger systems can be studied. Computational methods are only models, and there is no advantage in rigorously solving Schrodinger's equation for a large system if that system has had to be abbreviated in order to make the calculations tractable. Semiempirical methods are thus seen to be well balanced: they are accurate enough to have useful predictive powers, yet fast enough to allow large systems to be studied.

All five semiempirical methods contain sets of parameters. For MINDO/3 atomic and diatomic parameters exist, while MNDO, AM1, PM3, and MNDO-d use only single-atom parameters. Not all parameters are optimized for all methods; for example, in MINDO/3, MNDO and AM1 the two electron one center integrals are normally taken from atomic spectra. In the list given in following Table, parameters optimized for a given method are indicated by ' . '. A '+' indicates that the value of the parameter was obtained from experiment (not optimized). Where either symbol is given, the associated parameter is not used in that method.

All five semiempirical methods also use two experimentally determined constants per atom: the atomic mass of the most abundant isotope and the heat of atomization.

CAChe Software

CAChe is a computer-aided molecular design (CAMD) modeling tool for the Microsoft® Windows ME, Microsoft® Windows 98 or Microsoft® Windows NT 4.0 operating systems. CAChe enables us to draw and model molecules and perform calculations on a molecule to discover molecular properties and energy values.

CAChe uses computational chemistry as an essential part of computer-aided chemistry. By applying computational molecular models derived from mathematical equations to a chemical sample we create, we can calculate molecular properties such as the position and behavior of electrons, and nuclei in certain conditions.

The computational chemistry tools that CAChe uses are derived from classical mechanics and quantum mechanics, and are applied to the chemical sample by a number of computational applications that perform calculations based on specified parameters.

Approximation used: - MNDO, MINDO/3, AM1, PM3, & MNDO-d

All five methods are similar enough to describe simultaneously. In the following discussion, applications specific to each method will be indicated in the text. This will allow easy comparison among the methods, a comparison, which is not obvious from their names. MINDO/3 stands for Modified Intermediate Neglect of Differential Overlap, version 3. MNDO stands for Modified Neglect of Diatomic Overlap, and AM1 is Austin Model 1; these are the first two of the MNDO-type methods. PM3 is the Modified Neglect of Diatomic Overlap, Parametric Method Number 3, and MNDO-d, is really just MNDO with d orbitals.

Earlier methods, such as CNDO (Complete Neglect of Differential Overlap) ignored all terms involving two different atomic orbitals on one atom. Because of this, CNDO was an example of a ZDO (Zero Differential Overlap) method.

MNDO, AM1, PM3, and MNDO-d belong to the family of NDDO (Neglect of Diatomic Differential Overlap) methods. In these methods all terms arising from the overlap of two atomic orbitals, which are on different centers or atoms are set to zero.

PM3 Method (Development and Importance)

The most important one electron semiempirical MO method for non-planar molecule is the extended Huckel theory. Wolfsberg and Helmholtz used an early version in treating the inorganic complex ions. The method was further developed and widely applied by Hoffman^[10-13]. The EH method was found to give rather accurate bond angles for molecules whose bonds are not highly polar, but to fail in bond angle prediction for molecules with very polar bonds. The EH method is not reliable for predicting bond length, dipole moment and barriers to internal rotation. The EH method is unreliable for predicting molecular conformation^[14]. Because the EH method gives poor predictions of such molecular properties, Jug concluded that this method is obsolete^[15].

To avoid certain limitations of EH method, Popel et al proposed the CNDO method in 1965. This method is SCF MO method and uses the ZDO approximation for all pairs of AOs, in overlap and electron-repulsion integrals. The INDO method is an improvement of CNDO method proposed by Pople, Beveridge and Dobosh in 1967; this is also SCF MO method. In INDO, differential overlap between AOs, on the same atom is not neglected in one-center electron-repulsion integrals, but is still neglected two-center electron-repulsion integrals. The CNDO and INDO methods

give fairly good bond lengths and bond angles, somewhat erratic dipole moments and poor dissociation energies.

The neglect of diatomic differential overlap (NDDO) method (suggested by Pople, Santry and Segal, 1965) is an improvement of INDO in which differential overlap is neglected only between AOs centered on different atoms. The degree of neglect of differential overlap in NDDO is more justifiable than CNDO and INDO. The NDDO method satisfies the rotational and hybridization invariance conditions without the need to use a common value for electron repulsion integrals involving different valence atomic orbitals on a given atom. A few initial attempts to parameterizing the NDDO method gave results that were rather disappointing^[16], and the method was little used until 1977 when Dewar and Thiel modified it to give the MNDO method.

Pople's aim in the CNDO and INDO method was to reproduce as well as possible the results of minimal-basis-set ab initio SCF MO calculations with theories requiring much less computer time than ab initio calculations. Since CNDO and NDDO use approximations, we can expect their results to be similar but less accurate than minimal-basis ab initio SCF results. Thus these methods do pretty well on molecular geometry but fail for binding energies. Dewar and coworkers devised several semiempirical SCF MO theories that closely resemble the INDO and NDDO methods. The semiempirical theories, which follow Dewar's approach to parameterization, will be called Dewar type theories. These theories treat only the valence electrons, and most of these theories use a minimal basis set of valence Slater type s and p AOs to expand the valence electron MOs. The Dewar type theories treat the molecule as a collection of valence electron and atomic cores, where each core consists of an atomic nucleus and the inner shell electrons.

The first useful Dewar type theory was the MINDO/3 (third version of modified INDO) method^[17-19], which has been parameterized for compounds containing C, H, O, N, B, F, Cl, Si, P and S. The average absolute error in MINDO/3 calculated properties are 11 Kcal/mol in heat of formation, 0.022 Å in bond lengths, 5.6° in bond angles, 0.49 D in dipole moment and 0.7 eV in IP^[1]. Large errors in heat of formation occur for small ring compounds, compounds with triple bonds, aromatic compounds, boron compounds and molecules with lone pairs.

MINDO/3 is based on the INDO approximation. Because MINDO/3 did not meet Dewar's aim, Dewar and Thiel developed the MNDO method²⁰⁻²². MNDO method has been parametrized for compounds containing H, Li, Be, B, C, N, O, F, Al, Si, Ge, Sn, Pb, P, S, Cl, Br, I, Zn and Hg. MNDO gives improved results than MINDO/3. For the same sample the absolute error are 6.3 Kcal/mol in heat of formation, 0.014 Å in bond lengths, 2.8° in bond angles, 0.30 D in dipole moment and 0.5 eV in IP.

In 1985 Dewar and coworkers published an improved version of MNDO called AM1 (Austin model 1, named for University of Texas at Austin)^[31]. AM1 has been parameterized for H, B, C, Al, Si, Ge, Sn, Pb, P, S, Cl, Br, I, Zn and Hg. The only difference in MNDO and AM1 are that the valence orbitals s and p on the same atom are allowed to differ.

Parameters used in Semiempirical Methods

Parameter	Description	MINDO/3	MNDO	AM1	PM3
U_{ss} and U_{pp}	s and p atomic orbital one-electron one-center integrals	+	*	*	*
β_s and β_p	s and p atomic orbital one-electron two-center resonance integral terms		*	*	*
I_s	s atomic orbital ionization potential for two center resonance integral term	+			
I_p	p atomic orbital ionization potential for two center resonance integral term	+			
β_{AB}	Diatomic two center one-electron resonance integral multiplier	*			
ξ_s	s -type Slater atomic orbital exponent	*	*	*	*
ξ_p	p -type Slater atomic orbital exponent	*	*	*	*
α_A	Atom A core-core repulsion term		*	*	*
α_{AB}	Atoms A and B core-core repulsion term	*			
G_{ss}	s-s atomic orbital one center two electron repulsion integral	+	+	+	*
G_{sp}	s-p atomic orbital one center two electron repulsion integral	+	+	+	*
G_{pp}	p-p atomic orbital one center two electron repulsion integral	+	+	+	*
G_{p^2}	p-p ¹ atomic orbital one center two electron repulsion integral	+	+	+	*
H_{sp}	s-p atomic orbital one-center two-electron exchange integral	+	+	+	*
K_{n_A} or a_{n_A}	A Gaussian multiplier for n th Gaussian of atom A			*	*
L_{n_A} or b_{n_A}	A Gaussian exponent multiplier for n th Gaussian of atom A			*	*
M_{n_A} or c_{n_A}	A Radius of center of n th Gaussian of atom A			*	*

In 1989, Stewart reparameterized AM1 to give the PM3 method (parameterized method 3, 1 and 2 being MNDO and AM1)^[6,20,21]. PM3 differs from AM1 as follows-

The one-center electron-repulsion integrals are taken as parameters to be optimized. The core-repulsion function contains only two Gaussian terms per atom. PM3 has been parameterized for H, C, Si, Ge, Sn, Pb, N, P, As, Sb, Bi, O, S, Se, Te, F, Cl, Br, I, Al, Ga, In, Ti, Mg, Zn, Cd AND Hg.

Above discussions clearly states that PM3 is very valuable and important parameterization. Hence I used PM3 method for calculation.

Geometry Optimization

Many systematic mathematical procedures (algorithms) exist to find a local minimum of a function of several variables. These procedures will find a local minimum in E in the neighborhood of initially assumed geometry. The process of finding such a minimum is called Geometry Optimization or energy minimization. For a molecule with several conformations, one must repeat the local minimum search procedure for each possible confirmation, so as to locate the Global Minimum. For a large molecule, there may be too many confirmations for all of them to be examined. Moreover, the true-global minimum equilibrium geometry might correspond to a highly unconventional structure that might not think to be considered.

Some procedures to find local minimum in E require only repeated calculations of E at various values of its variables, but these procedures are very insufficient. More efficient procedures require repeated calculation of both E and its derivatives. The set of (3N-6) first partial derivatives of E with respect to each variable constitutes a vector (in a "space" of 3N-6 dimensions) called a gradient of E. at a local minimum; the gradient must be equal to zero. A point on the PES where the gradient is zero is called a stationary point. A stationary on the PES may be a minimum or maximum or a SADDLE POINT.

Analytical calculation of the gradient is key to efficient geometry optimization. The SCF energy expression is given as

$$E_{HF} = \sum_{i=1}^{N/2} E_i + 1/2 \sum_{r=1}^b \sum_{s=1}^b P_{rs} H_{rs}^{core} + V_{N,N}$$

and its derivative w.r.t. nuclear coordinates would seem to involve the derivatives of the H_{rs} and (rs/tu) integrals (which occur in E_i), the derivatives of V_{NN} . The derivatives of integrals are readily calculated, since the derivative of a Gaussian type function with respect to nuclear coordinate is another GTF. The derivatives of V_{NN} are trivial. Thus an analytical formula for the gradient of SCF energy is known. Once the SCF energy E and wave function have been found for some chosen geometry, the time needed to analytically calculate the energy gradient is roughly equal to the time needed to do the SCF wave function and energy calculation.

As well as using the energy gradient (the 3N-6 first partial derivatives $\partial E/\partial q_1, \partial E/\partial q_2, \dots$), some energy minimization methods also use the second derivatives of E. The set of second derivatives.

$$\partial^2 E/\partial q_1^2, \quad \partial^2 E/\partial q_1 \partial q_2, \quad \partial^2 E/\partial q_2^2$$

When arranged in square array from a matrix called the HESSIAN or the force constant matrix (since the second derivatives of E are force constants). An efficient way to find local minimum of a function of several variables is the Newton Method, which approximates the function by Taylor-series expressions, that is terminated after quadratic terms, and uses accurately evaluated first and second partial derivatives of the function (which occur in the linear and quadratic terms of the Taylor-series),

because the analytical calculation of the second derivatives in an SCF calculation is very costly in computer time. The SCF-geometry optimization commonly uses a modification of Newton procedure called quasi-Newton method.

The most frequently employed geometry optimization schemes are those of Mc Iver and Komornicki^[23-25] and force method due to Pulay^[26-28]. The Mc Iver and Komornicki method utilizes the minimization algorithm of Murgath and Sargent, a quadratically convergent method which preserves the molecular symmetry during calculations.

The optimization method developed by Pulay is based on Newton–Raphson minimization algorithm. This method requires some approximation to force constant matrix κ , which is assumed to be diagonal. From this matrix and the forces calculated at some initial geometry, a new geometry is generated and the whole process is repeated until the final forces become negligibly small. Force constant calculations require the determination of forces in the neighborhood of the equilibrium. If the i^{th} force F_i is changed by ΔF_i arising from internal coordinate change Δq_j , then

$$K_{ij} = - \Delta F_i / \Delta q_j$$

This is known as the force method and was used within the CNDO/2 approximation by Pulay *et al.*^[29-30]. There are several applications of this method at *ab initio* level^[31-37].

The force method appears the far more accurate than the straight–forward calculation of force constants via numerical differentiation to the total energy. The latter method, which is widely employed for large molecules, requires the calculation of total energy of selected geometries. Then either, directly or indirectly, some polynomial expression to the energy hyper surface is performed and corresponding second order derivatives are obtained. The analytical form of the polynomial is sensitive both to the assumed grid. The accuracy of polynomial approximation depends also on the precise q dependence on energy. However, the method is computationally simple, only requiring standard energy calculations to be repeated several times. As long as the cost of a single calculation is fairly low the method will be sufficiently inexpensive. For this reason, this brute force scheme is frequently employed within PM3 calculations.

Stretching force constants (for which the internal vibrational energy coordinates is the change in bond length) and bending force constants (for which the internal coordinate is the change in valance angle) are most commonly calculated and the diagonal force constants, K_{ij} , are usually computed. However, some attempts at a complete prediction of the whole set of the force constants and vibration frequencies do exist^[38].

Multi linear Regression Analysis

Multi linear Regression attempts to model the relationship between two or more explanatory variables and a response variable by fitting a linear equation to observed data. Every value of the independent variables and a response variable by fitting a linear to observed data. Every value of the independent variable χ is

associated with a value of the dependent variable y . The population regression line for p explanatory variables x_1, x_2, \dots, x_p is defined to be

$$\mu_y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_p x_p$$

This line describes how the mean response μ_y changes with the explanatory variables. The observed values for y vary about their means μ_y and are assumed to have the same standard deviation σ . The fitted values b_0, b_1, \dots, b_p estimate the parameters $\beta_0 + \beta_1 + \dots + \beta_p x_p$ of the population regression line.

Since the observed values for y vary about their means μ_y , the multiple regression model included a term for this variation. In words, the model is expressed as DATA = FIT + RESIDUAL, where the "FIT" term represents the expression $\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_p x_p$. The "RESIDUAL" term represents the deviations of the observed values y from their means μ_y , which are normally distributed with mean 0 and variance σ . The notation for model deviation is ϵ .

Formally, the model for multiple linear regressions, given n observations, is

$$y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \dots + \beta_p x_{ip} + \epsilon_i \text{ for } i = 1, 2, \dots, n.$$

In the least squares model, the best-fitting line for the observed data is calculated by minimizing the sum of the squares of the vertical deviations from each data point to the line (if a point lies on the fitted line exactly, then its vertical deviation is 0). Because the deviations are first squared, then summed, there are no cancellations between positive and negative values. The least-squares estimates b_0, b_1, \dots, b_p are usually computed by statistical software.

The values fit by the equation $b_0 + b_1 x_{i1} + \dots + b_p x_{ip}$ are denoted \hat{Y}_i , and the residuals e_i are equal to $y_i - \hat{Y}_i$ the difference between the observed and fitted values. The sum of the residuals is equal to zero.

The variance σ^2 may be estimated by $s^2 = \sum e_i^2 / (n-p-1)$, also known as the mean-squared error (or MSE). The estimate of the standard error s is the square root of the MSE.

Definition of quantum mechanical descriptors

Following quantum mechanical descriptors have been used for QSAR analysis-

1. Heat of Formation
2. Molecular Weight
3. Total Energy
4. HOMO Energy
5. LUMO Energy
6. Absolute Hardness
7. Electronegativity

The evaluation of these parameters is given as below-

In DFT the ground state energy of an atom or a molecule is written in terms of electron density $\rho(r)$, and the external potential $v(r)$ in the form^[39]

$$E(\rho) = F(\rho) + \int dr \rho(r) v(r), \quad 1$$

Where $F(\rho) = T(\rho) + V_{ee}(\rho)$, $T(\rho)$ is the electronic kinetic energy functional, and $V_{ee}(\rho)$ is the electron-electron interaction energy functional. The minimization of the total energy, subject to the condition that the total number of electrons is fixed,

$$N = \int dr \rho(r) \quad 2$$

Leads to an Euler-Lagrange equation of the form,

$$\mu = (\partial E / \delta \rho(r))_v = v(r) + \partial F / \delta \rho(r), \quad 3$$

where μ , the Lagrange multiplier, is the chemical potential. The solution of this equation leads to the ground state density, from which one can determine the ground state energy. Parr et al define the electronegativity as the negative of chemical potential.

$$\chi = -\mu = -(\partial E / \partial N)_v \quad 4$$

Although the Hard & Soft Acids and Bases concept was introduced more than three decades ago by Pearson, the first unambiguous definition of Hardness and Softness was given by Parr and Pearson in early 80s^[40] they defined global Hardness η as

$$\begin{aligned} \eta &= 1/2(\delta\mu/\delta N)_{v(r)} \\ &= 1/2(\delta^2 E / \delta^2 N)_{v(r)} \end{aligned} \quad 5$$

where E is the total Energy, N the number of electrons of the chemical species and $v(r)$ the external potential.

The corresponding global softness S , which bears an inverse relationship with the global hardness, is defined as^[41]

$$S = 1 / 2\eta = (\partial N / \partial \mu)_{v(r)} \quad 6$$

The operational definition of global hardness and global softness are obtained by finite difference approximation of eq-1^[42] ?

$$\eta = 1 / 2 (IP-EA) \quad 7$$

$$S = 1 / (IP-EA) \quad 8$$

where IP and EA are the Ionization Potential and Electron Affinity respectively, of the chemical species. According to the Koopman's theorem the IP is simply the eigen value of HOMO with change of sign and EA is the eigen value of LUMO with change of sign^[43], therefore on this basis we can write

$$\eta = \frac{1}{2} (\epsilon \text{ LUMO} - \epsilon \text{ HOMO}) \quad 9$$

$$S = 1 / (\epsilon \text{ LUMO} - \epsilon \text{ HOMO}) \quad 10$$

$$\chi = \frac{1}{2} (\epsilon \text{ LUMO} + \epsilon \text{ HOMO}) \quad 11$$

$$\mu = -\frac{1}{2} (\epsilon \text{ LUMO} + \epsilon \text{ HOMO}) \quad 12$$

→ more
disturb

References

1. Parr, R. G.; Donnelly, R. A.; Levy, M.; Palke, W. E.; *J. Chem. Phys.*, **1978**, *68*, 3801.
2. Sanderson, R. T.; *Chemical Bonds and Bond Energy*, Academic, New York, **1976**.
3. Dewar, M. J. S.; Thiel, W.; *J. Am. Chem. Soc.*, **1977**, *99*, 4899–4907.
4. Bingham, R. C.; Dewar, M. J. S.; Lo, D. H.; *J. Am. Chem. Soc.*, **1975**, *97*, 1285–1293.
5. Dewar, M. J. S.; Zoebisch E. G.; Healy, E. F.; Stewart J. J. P.; *J. Am. Chem. Soc.*, **1985**, *107*, 3902–3909.
6. Stewart, J. J. P.; *J. Comp. Chem.*, **1989**, *10*, 209–220.
7. Thiel, W.; Voityuk, A.; *Theor. Chem. Acta.*, **1992**, *81*, 391–404.
8. Thiel, W.; Voityuk, A.; *J. Phys. Chem.*, **1996**, *100*, 616–629.
9. Baker, J.; *J. Comp. Chem.*, **1986**, *7*, 385.
10. Hoffmann, R.; *J. Chem. Phys.*, **1963**, *39*, 1397.
11. Hoffmann, R.; *J. Chem. Phys.*, **1964**, *40*, 2745.
12. Hoffmann, R.; *Tetrahedron*, **1966**, *22*, 521.
13. Wolfsberg, M.; Helmbolz, L.; *J. Chem. Phys.*, **1952**, *20*, 837.
14. Pullman, B.; *Adv. Quantm. Chem.*, **1977**, *10*, 251.
15. Jug, K.; *Theor. Chem. Acta.*, **1980**, *54*, 263.
16. Klopman, G.; Evnas, R. C.; Segal Part A, Chapter 2.
17. Bingham, R. C.; Dewar, M. J. S.; Lo, D. H.; *J. Am. Chem. Soc.*, **1975**, *97*, 1285.
18. Dewar, et al, *J. Am. Chem. Soc.*, **1975**, *97*, 1311.
19. Dewar, *Science*, **1975**, *187*, 1035.
20. Dewar, M. J. S.; Thiel, W.; *J. Am. Chem. Soc.*, **1977**, *99*, 4899.
21. Dewar, M. J. S.; Rzepa, H. S., *J. Am. Chem. Soc.*, **1978**, *100*, 58.
22. Dewar, M. J. S.; McKee, M. L.; *J. Am. Chem. Soc.*, **1977**, *99*, 5231.
23. Komornicki, A.; McIver, J. W.; *Chem. Phys. Lett.*, **1971**, *10*, 303.
24. Komornicki, A.; McIver, J. W.; *J. Am. Chem. Soc.*, **1972**, *94*, 2625–2633.
25. Flanigan, M. C.; Komornicki, A.; McIver, J. W.; *Modern Theoretical Chemistry*, Plenum Press, New York, Vol.8, **1977**.
26. Pulay, P.; *Mol. Phys.*, **1969**, *17*, 197.
27. Pulay, P.; *Modern Theoretical Chemistry, Vol-3, Applications of Electronic Structure Theory*, Plenum Press, New York, **1977**, p153.
28. Pulay, P.; Torok, F.; *Mol. Phys.*, **1973**, *25*, 1155.
29. Pulay, P.; Torok, F.; *J. Mol. Struct.*, **1975**, *29*, 239.
30. Pulay, P.; Meyer, W.; *Theoret. Chim. Acta.*, **1974**, *32*, 253.

31. Botschwina, P.; *Chem. Phys. Lett.* , 1974,29, 580.
32. Pulay, P.; *Mol. Phys.*, 1971, 21, 329.
33. Pulay, P.; Meyer, W.; *Mol. Phys.*, 1974, 27, 473.
34. Pulay, P.; Sawodny, W.; *Mol. Phys.*, 1975, 30, 1123.
35. Pulay, P.; Sawodny, W.; *J. Mol. Spectrosc.* ; 1974, 51, 135.
36. Torok, F.; Hedegus, A.; Kosa, K.; Pulay, P.; *J. Mol. Struct.* , 32, 93.
37. Panchenko, N. Y.; Pulay, P.; Torok, F.; *J. Mol. Struct.* , 34, 1976, 1976, 283.
38. Dewar, M. J. S.; Rzepa, H. S.; *J. Am. Chem. Soc.*, 1978, 100, 777.
39. Robert, G.; Parr and Yang Weitao. *Density-functional Theory of Atoms and Molecules* (Oxford University Press, 1994).
40. Parr , R.G.; Pearson, R.G.; *J. Am. Chem. Soc.* 1983,105, , 7512.
41. Yang, W.; Parr, R.G.; *Proc Natl. Acad. Sci. U.S.A.* 82, 1985 , 6723.
42. De Proft, F.; Langenaeker W.; Geerlings, P.; *J. Phys. Chem.*, 1993, 97, 826.
43. Pearson, R.G.; *Acc. Chem. Res.*, 1993, 26, 250-255.