

Chapter 13

Electrostatic Potential at Nuclei: An Accurate Reactivity Descriptor for Organic Compounds

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ABSTRACT

The chapter surveys mostly original work of the authors on the application of the electrostatic potential at nuclei (EPN) as a reactivity index in quantifying hydrogen bonding as well as different reactions of organic compounds. The EPN index was defined and introduced by E. B. Wilson (1962). However, it was first applied as a reactivity index much later in works from our laboratory (Bobadova-Parvanova & Galabov, 1998; Galabov & Bobadova-Parvanova, 1999; Dimitrova, Ilieva, & Galabov, 2002; Cheshmedzhieva, Ilieva, Hadjieva, Trayanova, & Galabov, 2009; Galabov, Cheshmedzhieva, Ilieva, & Hadjieva, 2004; Galabov, Ilieva, & Schaefer, 2006; Galabov, Nikolova, Wilke, Schaefer, & Allen, 2008; Galabov, Ilieva, Hadjieva, Atanasov, & Schaefer, 2008; Koleva, Galabov, Wu, Schaefer, & Schleyer, 2009).

Numerous applications showed that the EPN index, an accurate quantum mechanical quantity, predicts with remarkable accuracy the energy shifts accompanying hydrogen bonding. The theoretically evaluated EPN descriptor correlates also excellently with experimental and theoretically evaluated kinetic parameters for a number of important organic reactions. Based on these findings an efficient computational approach for the evaluation of substituent constants was developed.

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INTRODUCTION

In the report “Opportunities in Chemistry: Today and Tomorrow” (known as the “Pimentel Report”) published in 1985 as the result of a study of the National Academy of Sciences of the United States “to survey the chemical science” under the chairmanship of George C. Pimentel, priority was recommended to five research frontiers. The first was “Understanding Chemical Reactivity: ... to apply the full power of modern instrumental techniques and chemical theory to the clarification of factors that control the rates of reaction and to the development of new synthetic pathways for chemical change”. For organic chemistry, the quantitative characterization of reactivity is of key conceptual importance. It underlines the link between properties of reactants and their behavior in chemical interactions and supports the understanding of organic chemistry as a fully quantitative science. Since the pioneering works of Hammett (1937; 1938), the interpretation of organic reactivities has been in the focus of numerous studies. Quantum chemistry has open new perspectives in understanding the factors governing chemical reactivity (Carey & Sanders, 2000; Fukui, 1975; Klopman, 1974; Parr & Yang, 1989; Streitwieser, 1961). In recent times, the introduction of reactivity indices, defined in the framework of density functional theory, has contributed greatly in understanding the factors governing the rates of chemical reactions (Chattaraj, 2009; Pearson, 1997; Sen & Jorgensen, 1993; Toro-Labbe, 2006). In spite of the impressive progress, achieving a quantitative accord between theoretical predictions and experimental kinetic rates is still a challenging task. It is, therefore, paramount to characterize chemical reactivity by analyzing the correspondence between theory and experiment.

In this chapter we describe the application of the electrostatic potential at nuclei, a non-approximate quantum mechanical quantity, in quantifying reactivity of molecules for intermolecular interac-

tions (hydrogen bonding) and several reactions of organic compounds. Comparisons with alternative approaches for reactivity predictions is made for all studied processes

Parallel to EPN we will also summarize results from the application of alternative theoretically derived reactivity indices, variously defined atomic charges, and the Parr electrophilicity index (ω) (Parr, Szentpály, & Liu, 1999), in a comparative approach. In the first section we present results on the application of EPN and atomic charges in quantifying reactivity of several series of molecules for processes of hydrogen bonding. In the second section we discuss chemical reactivities in several important organic reactions. The third part shows the successful application of the electrostatic potential at nuclei in quantitatively predicting substituent constants for aromatic systems.

BACKGROUND

An important theoretical quantity employed in analyzing chemical reactivity is the molecular electrostatic potential (MEP) (Scrocco & Tomasi, 1973; Politzer & Truhlar, 1981; Murray & Politzer, 1988; Murray, Lans, Brinck, & Politzer, 1991; Tomasi, Bonaccorsi, & Cammi, 1990; Gadre, Kulkarni, & Srivastava, 1992; Murray & Sen, 1996; Naray-Szabo & Ferenczy, 1995; Suresh & Gadre, 1997; Suresh & Gadre, 2007). Minima and maxima of the surface MEP have been widely used in studying the structural factors determining the relative rates of various intermolecular interactions. Extensive surveys on the subject are available (Scrocco & Tomasi, 1973; Murray & Politzer, 1988; Murray & Sen, 1996; Naray-Szabo & Ferenczy, 1995; Politzer & Truhlar, 1981; Tomasi, Bonaccorsi, & Cammi, 1990). The great advantage of MEP over alternative theoretical approaches in analyzing reactivity is the fact that no additional approximations are introduced in deriving MEP. Thus, maps of MEP, typically at the Van der Waals surface of the molecule,

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