Tetrahedron Letters,Vol.23,No.10,pp 1027-1030,1982 0040-4039/82/101027-04$03.00/0
Printed in Great Britain

Reaction Potential Map Analysis of Chemical Reactivity

Gilles Klopman

Department of Chemistry, Case Western Reserve University
Cleveland, Ohio 44106, USA

Hideki Moriishi, Osamu Kikuchi, and Keizo Suzuki

Department of Chemistry, The University of Tsukuba
Sakura, Ibaraki 305, Japan

Abstract: Reaction potential maps (RPM) are proposed as a new kind of molecular reactivity index. They involve both the electrostatic and orbital interactions between reagents, and are potentially helpful in elucidating the site selectivity observed in a variety of chemical reactions.

The calculation of electrostatic potential maps (EPM) as a guide to the reactive regions of molecules was pioneered by Bonaccorsi et al.[1] The introduction of their methodology constituted a marked improvement over previous methods of analyzing the reactive sites of molecules and was quickly adopted as a major tool for the elucidation of reaction properties of biological compounds.[2] However, EPM involves only the electrostatic interactions between reagents, and its applicability is, therefore, strongly limited. Indeed, in their currently used form, these maps are drawn as functions of one of the substrates only and fail to include the effect of the other reagent. The ambident character of nucleophiles, such as SCN^-, for example, cannot be explained by Electrostatic Potential Maps. Furthermore, since the maps represent only potential energy fields, the effect of orbital symmetry is not represented in them.

The interaction energy between two species comprises not only electrostatic and polarization energies, but also exchange, charge transfer (function of orbital symmetry), and dispersion energies.[2] The equipotential energy maps involving all these components are functions of both reagents and display much more reactivity information than EPM alone. It is thus proposed that this kind of reagent dependent mapping, called hereafter reaction potential maps (RPM) could be more useful in exploring site selectivity and in predicting the reactivity of molecules toward different kinds of reagents.

In our proposed methodology, we gain a qualititative understanding of the general trends of molecular reactivity by drawing the RPM's resulting from the interaction between various reagents and the molecule to be investigated. So far, we have considered the attacking reagents to be single and localized atomic orbitals. For example, in the study of the reactivity of the SCN^-

anion, the model electrophile has a unitary positive charge and no electrons. Its empty 1s orbital receives an electron pair from the nucleophile by a charge transfer mechanism during the rate determining step. The interaction energy is calculated from the rigorous perturbation equations given by Murrell et al.,[3] and is obtained by summing up the energy components of the nucleophile(A)-electrophile(B) system:

$$E_{int} = E_Q + E_I + E_{CT}$$

$$E_Q = 2\sum_i V^B_{ii} + \Sigma Z_a e^2/R_{aB}$$

$$E_I = 2\sum_{ik}\sum \{V^B_{ik}\}^2/(\varepsilon_k - \varepsilon_i - \langle ii|kk\rangle + 2\langle ik|ki\rangle)$$

$$E_{CT} = 2\sum_i \{V^B_{ib} - S_{ib}V^B_{ii}\}^2/(\varepsilon_b - \varepsilon_i)$$

where V^B_{pq} is the core attraction energy between the positive charge of the model particle and the electron density $\phi_p\phi_q$, and i and k are occupied and unoccupied MO's of the nucleophile, respectively. E_Q is identical with the electrostatic potential energy used in the EPM study of a molecule against a proton.[1,2]

Notice that the perturbation term is valid only as long as the overlap between the reacting species remains small. Thus the RPM's become meaningless at the vicinity of the atoms and boundary conditions must be carefully defined. So far, we have not found an absolute criterion for defining such boundaries and for the present have arbitrarily selected the region where the electrostatic potential is negative, i.e. the EPM boundary, as that where the RPM calculations are believed to be valid.

Two typical values were adopted for the orbital energy, ε_b, of the empty Slater 1s orbital of the electrophile; 0 eV for the soft electrophile and +6eV for the hard electrophile. The behavior of soft electrophiles is illustrative

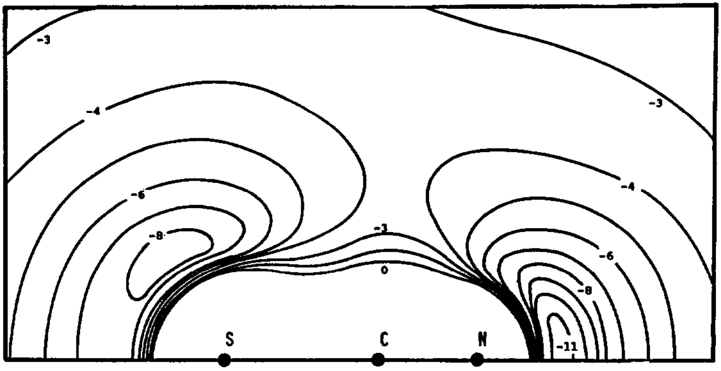
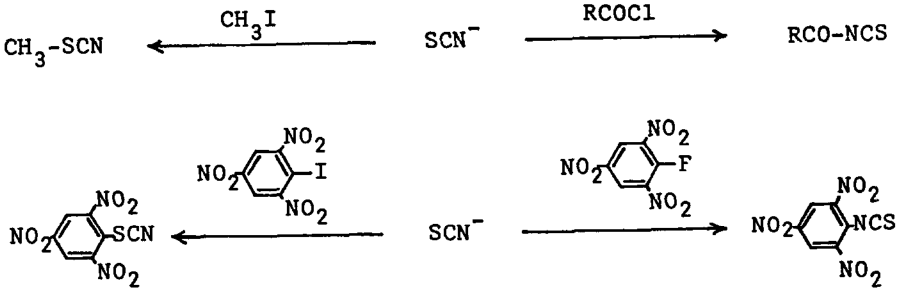


Figure 1. Electrostatic Potential Map of SCN⁻. Values are in eV.

of what can be expected from inorganic reagents such as Ag^+ and Zn^{2+} and organic reagents such as saturated carbon-iodine or carbon-bromine bonds while the hard electrophiles represent electrophiles such as Ti^{+4}, Mg^{+2}, carbonyl derivatives, saturated carbon fluorine bonds, etc...[4] Figures 1 and 2 show the EPM and RPM's of SCN^- calculated by using CNDO/2 wavefunctions. In EPM (Fig. 1), two energy minimum regions are observed near the S and N atoms. These come from the large negative charges on the S and N atoms. The deeper minimum at the N region indicates that electrophiles react preferably at the N atom. However, it has been observed experimentally[4] that SCN^- forms isothiocyano derivatives with hard electrophiles whereas it binds as a thiocyano compound with soft electrophiles. This ambident character of SCN^- cannot be elucidated by the EPM.



In the RPM of SCN^- with hard electrophiles (Fig. 2a), the minimum regions are shifted slightly from the EPM regions. This shift is due to the partial transfer of electrons from the sulfur 3p lone-pair orbitals (degenerate HOMO's) to the empty orbital of the electrophile. This charge transfer interaction is recognized remarkably in the RMP obtained for the soft electrophile (Fig. 2b) whose empty orbital is lower than that of the hard electrophile. In this case, the potential energy well near the S atom becomes deeper than that near the N atom, and this suggests that the SCN^- anion can be attacked at the S atom rather than the N atom by soft electrophiles.

It is thus found that the RPM's of SCN^- represent well its ambident nucleophilic character. RPM's involve both the charge and orbital interactions and, therefore, reproduce the ambident character of nucleophiles which cannot be explained by EPM. In this preliminary study, the RPM analysis employs a model particle for the attacking electrophile. By adopting an appropriate model for other reagents the methodology can easily be used to study a large variety of reactions. A 1s orbital occupied by a pair of electrons, for example, can be used as a model for nucleophiles. Detailed calculation procedure of the present RPM analysis as well as the RPM's of SCN^- and related nucleophiles will be reported shortly.

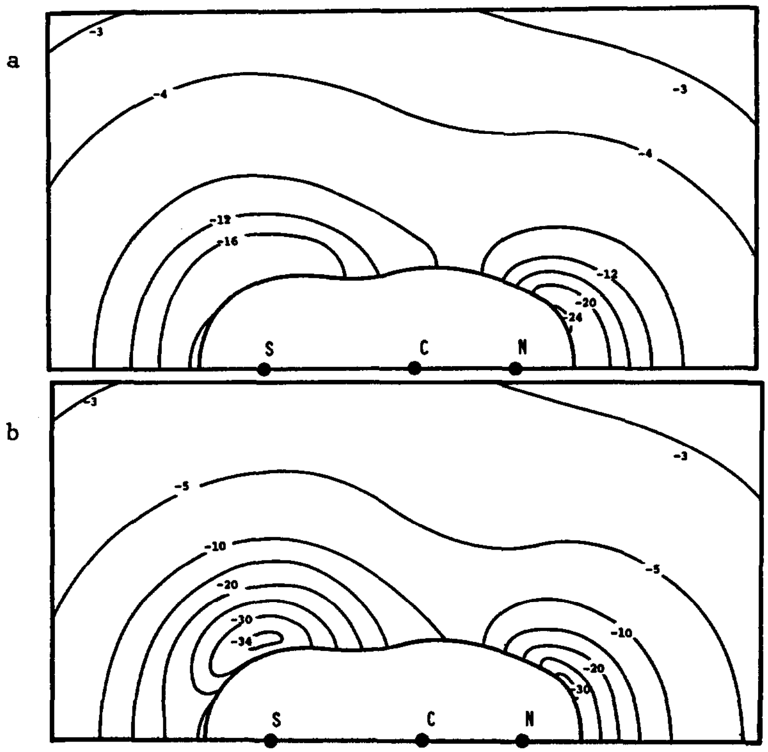


Figure 2. Reaction Potential Maps of SCN$^-$ towards the (a) hard and (b) soft Electrophiles. Values are in eV.

References

1. R. Bonaccorci, E. Scrocco, and J. Tomasi, J. Chem. Phys. 52, 5270 (1970).
2. For review and discussion on the electrostatic potential maps, see: (a) J. Tomasi, "Quantum Theory of Chemical Reactions, I," ed. by R. Daudel et al., Reidel, Dordrecht (1980), p. 191. (b) P. Politzer and K. C. Daiker in "The Force Concept in Chemistry," ed. by B. M. Deb, Van Nostrand Reinhold, N.Y. (1981), ch. 6.
3. J. N. Murrell, M. Randic, and D. R. Williams, Proc. Roy Soc., A284, 566 (1965).
4. G. Klopman, "Chemical Reactivity and Reaction Paths," Wiley-Intersci., New York (1974), p. 77; D. E. Giles and A. J. Parker, Aust. J. Chem. 26, 273 (1973).

(Received in USA 16 October 1981)