Tetrahedron Letters,Vol.24,No.25,pp 2541-2544,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

RESIDUAL ELECTRONEGATIVITY - AN EMPIRICAL QUANTIFICATION OF POLAR INFLUENCES AND ITS APPLICATION TO THE PROTON AFFINITY OF AMINES

Michael G. Hutchings and Johann Gasteiger*

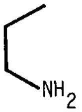
Organisch-Chemisches Institut, TU München, D-8046 Garching, West Germany

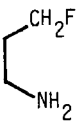
The residual electronegativity of an atom in a molecule can be used as a quantitative measure of the polar influence of a substituent on reactivity, as exemplified by its ability, with substituent polarisability, to correlate the proton affinity data of 80 amines.

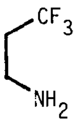
A cornerstone of organic chemistry is the notion that there exist fundamental relationships between the structure of a molecule and its chemical reactivity. Concepts like inductive, resonance, steric, polarisability and solvent effects have been invoked in a qualitative manner, whereas the quantitative treatment has centred around linear free energy relationships (LFER). With LFER, correlations are sought between two sets of reactivity data, the reaction under investigation, and a standard one. Although this empirical approach has been quite successful some serious problems still exist. The artificial separation of a structure into substituent, skeleton and reaction site has critical consequences:

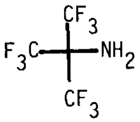
1. Interactions between these molecular subunits in the two sets of reactions have to be comparable. That is, each component of the overall interaction (e.g., resonance, inductive) should be of equal weighting in the two systems. This has led to a proliferation of standard reaction systems and to a host of different tables of substituent constants as well as to dual substituent parameter schemes.[1]
2. Sets of compounds that encompass different skeletons within one series cannot be studied.
3. For sets of molecules with several substituents additivity of effects has to be assumed to allow an LFER treatment.

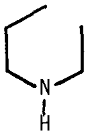
These problems clearly show up when trying to find a quantitative description of proton affinity (PA) data of amines comprising molecules of different skeletal and substitution types, e.g.

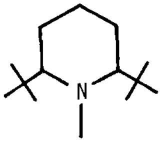












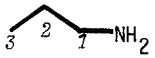
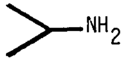
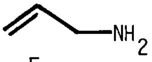
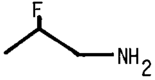
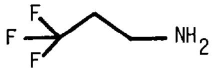
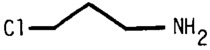
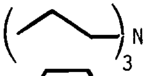
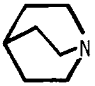
A solution to these problems can only be found by treating each molecule as an individual entity.

One approach is the application of quantum mechanical methods. However, we wished to retain traditional concepts, such as inductive effect, within the framework of a rapid, empirical but quantitative treatment. In other words, we were seeking to find a simple way to quantify inductive effects for systems of different skeletal and substitution types.

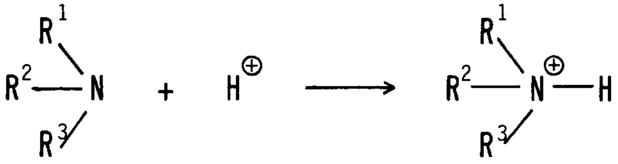
A recent paper has described an iterative procedure for the rapid calculation of atomic charges within a molecule, dependent on partial equalisation of orbital electronegativity.[2] Implicit in this procedure is the result that each atom ends up not only with a uniquely defined charge value, but also with a final, residual electronegativity (RE) value - "residual" in the sense that this electronegativity reflects the remaining ability of the particular atom in the molecular environment to attract (negative) charge towards itself.

The main characteristics are illustrated with results on the amines contained in the table:

- Nonequivalent atoms of the same elemental type in a molecule have different RE (e.g., the three carbon atoms in 1).
- Branching effects are taken into account (cf. 1 and 2).
- Atoms with different hybridisation states have different RE (cf. 1 and 3).
- The influence of heteroatoms is taken into account reflecting the *magnitude* of the inductive effect (cf. 1, 4 - 7).
- The position of a heteroatom makes a difference (cf. 4, 5). Thus the *attenuation* of the inductive effect is reproduced.
- Interactions between substituents are taken into account (6).
- Changes in the types of skeletons can be handled (cf. 8, 9).

		residual electronegativity			proton affinity [kJ/mole]	
		χ_3	χ_2	χ_1	exp	calc
1		7.40	7.58	7.91	914.2	913.8
2		7.52	7.52	7.97	918.0	918.0
3		7.86	8.08	8.08	905.8	908.3
4		7.68	9.02	8.20		895.5
5		8.83	7.87	7.94	915.0	906.3
6		11.86	8.49	7.99	886.2	896.6
7		8.20	7.73	7.93	913.8	912.5
8		7.40	7.59	7.97	976.5	978.2
9		7.64	7.64	7.97	968.2	961.9

Thus, the concept of RE opens the way for a quantitative definition of the inductive effect and its application in reactivity studies. We now exemplify the use of RE in one such system, that of the gas phase proton affinity (PA) of aliphatic amines, equation 1 .



(1)

$PA = -\Delta H_r(1)$

R^1, R^2, R^3 = H, alkyl, heterosubstituted alkyl

It has been concluded that PA is dependent both on polar (inductive/field) effects of substituents, and polarisability effects.[3] In the preceding paper, we have introduced quantitative models for the latter, and shown that in near absence of polar effects, the PA of a series of 49 unsubstituted alkylamines correlate well with the polarisability values.[4] The value of RE as a quantitative descriptor of polar effects is reflected when the study is extended to include amines, both saturated and unsaturated, primary, secondary and tertiary, as well as containing N, O, F, Cl and Si in the substituents.[3,5] A dual parameter scheme (eq. 2) suffices to give a good overall correlation for 80 amines extending from 795 kJ/mole for $t\text{-}C_4F_9NH_2$ to 1000 kJ/mole for 2,6-di-t-butyl-N-methylpiperidine[6] (Figure).

$$PA = 1435.5 - 116.3\ \chi_S + 12.5\alpha_d \qquad (2)$$

α_d is the effective polarisability, calculated as described previously.[4] χ_S is a composite residual electronegativity term given by $\chi_S = 0.5\ (\overline{\chi_1} + 0.25\overline{\chi_2})$ where $\overline{\chi_1}$ is the mean RE of the atoms directly bonded to the amine N-atom, and $\overline{\chi_2}$ is the mean RE of atoms one bond sphere further out. This simple function provides somewhat better results then either $\overline{\chi_1}$, $\overline{\chi_2}$ or the nitrogen RE itself. For the species contained in the table, the values for the PA calculated by eq. 2 are given and compared with experimental data. Note that this eq. can also be used in a predictive manner, as for compound <u>4</u>.

Each of the two parameters needed in the regression analysis is chemically meaningful and intuitively understandable. Thus, the fact that the electronegativity term is associated with a negative coefficient is a reflection of the obvious fact that increasingly electronegative substituents provide decreasingly good positive charge stabilisation. Additionally, the positive sign of the polarisability coefficient is consistent with increasing polarisability always acting to stabilise charge development.

Earlier analyses have applied conventional substituent constants of the Hammett/Taft variety to restricted series of molecules.[7] As far as we are aware, this is the first quantitative treatment of amine PA which includes such a large range of substitution types. We therefore believe that the approach introduced in this communication provides a powerful alternative which circumvents problems inherent in the use of substituent constants, while nevertheless being conceptually related to the latter.

We have used only the amine PA reaction to exemplify this new method; the RE/substituent polarisability approach has been applied successfully to many other reaction systems, as we shall report elsewhere.

We thank the Organics Division of I.C.I. Plc for financial support.

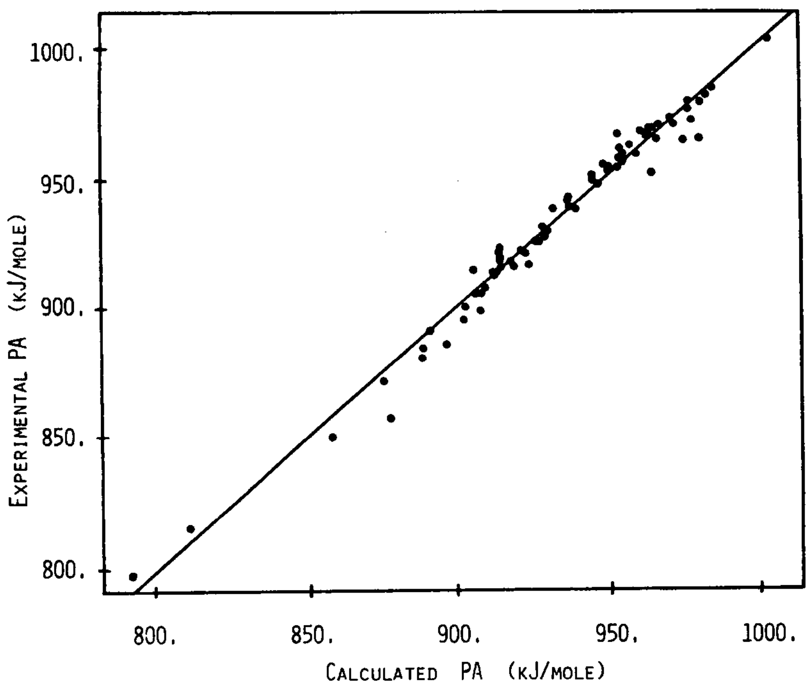


Figure: Experimental and calculated (eq. 2) proton affinities of amines (primary, secondary and tertiary, as well as those bearing N, O, F, Cl, Si in the substituents)

References

1. N.B. Chapman and J. Shorter, "Advances in Linear Free Energy Relationships", Plenum Press, 1972; "Correlation Analysis in Chemistry", Plenum Press, London, 1978.
2. J. Gasteiger and M. Marsili, Tetrahedron, 1980, 36, 3219; Tetrahedron Lett., 1978, 3181.
3. D.H. Aue and M.T. Bowers, in "Gas Phase Ion Chemistry", ed. M.T. Bowers, Academic Press, New York, 1979, vol. 2, p. 1.
4. J. Gasteiger and M.G. Hutchings, preceding paper.
5. K.N. Hartman, S. Lias, P. Ausloos, H.M. Rosenstock, S.S. Schroyer, C. Schmidt, D. Martinsen and G.W.A. Milne, "A Compendium of Gas Phase Basicity and Proton Affinity Measurements", NBSIR 79-1777, U.S. Dept. of Commerce, Nat. Bur. of Standards, 1979.
6. J.C. Day, J. Am. Chem. Soc., 1981, 103, 7355.
7. R.W. Taft, M. Taagepera, J.L.M. Abboud, J.F. Wolf, D.J. DeFrees, W.J. Hehre, J.E. Bartmess, R.T. McIver, Jr., J. Am. Chem. Soc., 1978, 100, 7765; R.W. Taft and L.S. Levitt, J. Org. Chem., 1977, 42, 916.

(Received in Germany 14 March 1983)