Are Electrophilicity and Electrofugality Related Concepts? A Density Functional Theory Study
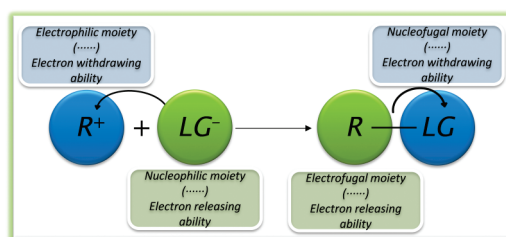
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ABSTRACT

It is proposed that the electrofugality of a fragment within a molecule is determined by its group nucleophilicity. The variation of electrofugality should be tightly related to the electron releasing ability of the substituent attached to the electrofuge moiety. This contribution closes the set of relationships between philicity and fugality quantities: while nucleofugality appears related to the group electrophilicity of the leaving group, electrofugality is related to the group nucleophilicity of the permanent group.

Electrophilicity,[1] nucleophilicity,[2] and their parent concepts nucleofugality[3] and electrofugality[4] provide useful information to understand polar processes and to explain reaction mechanisms in organic chemistry. Experimental scales of electrophilicity, nucleophilicity, nucleofugality, and electrofugality are now available for a significant number of molecules that participate in nucleophilic substitution and elimination reactions.[1c,2a,2b,3c,3d,4a]

Within the universal scale of Mayr et al.,[5] nucleophilicity (N) and electrophilicity (E) numbers are obtained from kinetic data using the following equation:

$$\log k_T = s(N + E) \tag{1}$$

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In eq 1, k_T is a second-order rate constant of the nucleophile−electrophile association recorded at temperature T, E is a nucleophile-independent electrophilicity parameter, and N and s are electrophile-independent and nucleophile-specific parameters, respectively.[5] The parent concepts nucleofugality (Nf) and electrofugality (Ef) are experimentally deduced from a similar expression, namely,

$$\log k_T = s_f (Nf + Ef) \qquad (2)$$

where the nucleofuge-specific parameters s_f and Nf refer to combinations of leaving groups with a reference nucleophile. Electrofugality is described by the single parameter Ef.[4b]

Recently, the electrofugality order for a series of four compounds (benzhydryl cations in interaction with phenylsulfinate) has been established using an inverse relationship between Ef and E parameters.[6] The resulting order of E was as follows: **17** > **18** > **19** > **20** (see Figure 1 for compound identification).
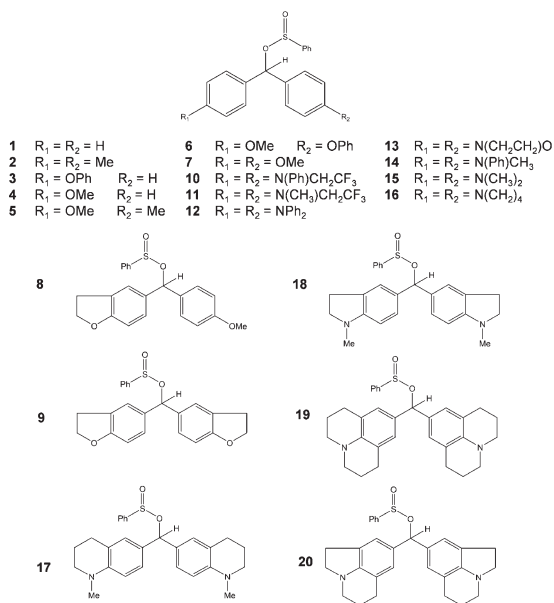

Figure 1. General structure of compounds used in the present study.

The relationship between $\log(k_2)$ and Ef for the interaction of benzhydrilium ions with phenylsulfinate is not linear: *the weakest electrophile is far from being the best electrofuge*.[6] In our opinion, this result is natural because electrofugality is more likely related to the group nucleophilicity of the permanent group rather than its global electrophilicity. The model is summarized in Scheme 1 below:

According to this scheme, the best electrofuge will be the fragment displaying the highest group nucleophilicity because during the process of heterolytic bond cleavage the electrofuge is expected to act as an electron donor moiety.

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Scheme 1. General Scheme for a Heterolytic Bond Cleavage Processes, Where R^+ Is the Electrofuge and LG^- Is the Nucleofuge
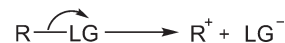
At the same time, the nucleofuge must display a high group electrophilicity to depart with the bonding electron pair.[3c] In other words, while electrophilicity and nucleophilicity are properties that refer to a molecule as a whole, electrofugality and nucleofugality are esentially group properties.[3c] The problem of experimentally evaluating regional properties is somehow hard, and it is at this point that theory may help to redefine them from theoretical models validated against observed quantities. In this Letter we show that the electrofugality pattern may be defined more accurately within a model based on the group nucleophilicity concept.[1a] The reliability of this proposal is validated against the experimental data recorded for a set of 20 benzhydryl sulfinate derivatives experimentally studied by Mayr et al.[6] They are depicted in Table 1.

Table 1. Experimental Electrophilicity E of the Benzhydryl Cations; Regional Nucleophilicity at Fragment R, N(R), and at Fragment LG, N(LG), in the Complex R-LG; Experimental and Predicted Electrofugality Ef of Benzhydryl Cations

Entry	E	N(R) (eV)	N(LG) (eV)	$\%N$(R)	Ef^b
1	5.90	−8.67	−0.08	99.1	−6.05
2	3.63	−8.37	−0.06	99.3	−3.47
3	2.90	−8.29	−0.03	99.6	−3.55
4	2.11	−8.16	−0.03	99.7	−2.06
5	1.48	−8.10	−0.03	99.6	−1.29
6	0.61	−8.13	−0.05	99.3	−0.81
7	0.00	−8.03	−0.04	99.5	0.00
8	−0.56	−7.94	−0.03	99.6	0.33^c
9	−1.36	−7.91	−0.04	99.5	0.60^c
10	−3.14	−7.75	−0.03	99.6	2.05^c
11	−3.85	−7.91	−0.03	99.6	0.63^c
12^a	−4.72	--	--	--	--
13	−5.53	−7.94	−0.03	99.6	0.36^c
14	−5.89	−7.38	−0.02	99.7	5.46^c
15	−7.02	−7.30	−0.02	99.7	6.22^c
16	−7.69	−7.02	−0.02	99.7	8.78^c
17	−8.22	−7.21	−0.02	99.7	6.99^c
18	−8.76	−7.30	−0.02	99.7	6.22^c
19	−9.45	−7.11	−0.02	99.7	7.91^c
20	−10.04	−7.17	−0.02	99.7	7.34^c

^{a} For this compound the algorithm used to evaluate the nucleophilic fukui function produces negative values. ^{b} Experimental electrofugality from ref 4b. ^{c} Predicted values using the empirical equation included in Figure 2b.

Such a model strongly demands an additivity rule for nucleophilicity in order to assess the fragment nucleophilicity which is being proposed here as a more general model of electrofugality. Theoretical values of group nucleophilicity may be readily obtained by defining the global

nucleophilicity (N) as the negative of ionization potential I[1a] and then projecting this value onto fragments using the condensed to atom k nucleophilic fukui function f_k^-, namely,

$$N^{\text{theoretical}} = -I \cong \varepsilon_{\text{HOMO}} \qquad (3a)$$

and

$$Ef^{\text{theoretical}} = N(R) = \sum_{k \varepsilon R} f_k^- \varepsilon_{\text{HOMO}} \qquad (3b)$$

In eqs 3a and 3b the vertical ionization potential has been approached using Koopmans theorem, in terms of the one-electron energy of the HOMO orbital.[7] Geometry optimization were performed at the HF/6-311G(d,p) level of theory, using the Gaussian 03 package of programs.[8] The nucleophilic Fukui function needed to project the local contributions was obtained from single-point calculations for the optimized structures using a method described elsewhere[9] at the HF/6-31G level of theory.

Inspection of Table 1 reveals that the global nucleophilicity of the R-LG complexes is almost concentrated at region R ($>99.0\%$), which within the present approach determines the electrofugality order. Note that the regional nucleophilicity at R is rationally ordered in terms of inductive substituent effects. For instance, the marginal electron donating ability of fragment R in the complex may be explained by Hammett σ substituent constants:[10] for compounds **1−5** the low electron donating ability of the fragment is determined by the presence of poor electron donor groups (H, Me). The electron donating ability of fragment R is smoothly increased in compounds **6−13**, probably as a result of the presence of better electron releasing groups (mainly oxygen and nitrogen containing

groups in combination with electron withdrawing atoms like F). The third group, compounds **13−20**, is predicted to be better nucleophilic R fragments due to the presence of nitrogen atoms in combination with alkyl groups.

The final validation is the comparison between the experimental electrofugality and the theoretical electrofugality described here by the $N(R)$ index. Such a comparison is shown in Figure 2 below.
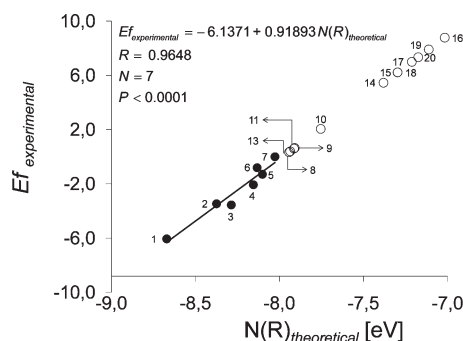
Figure 2. Comparison between experimental electrofugality ($\bullet$) and the regional nucleophilicity of the permanent group R for a series of benzhydryl phenyl sulfinates derivatives. Predicted electrofugality values are included ($\circ$).

Note that the experimental electrofugality values consistently correlate with the regional nucleophilicity of the permanent group and that such a comparison is this time linear. This linear relationship is expected to become a simple and useful tool to anticipate the electrofugality pattern within a series of related molecules. This is the case for compounds **17**, **18**, **19**, and **20** for which the predicted order of electrofugality, according to the present model, would be **19 > 20 ≈ 17 > 18**.

We have shown that the electrofugality pattern of a fragment within a molecule is related to its group nucleophilicity. The variation of group nucleophilicity is tightly related to the electron releasing ability of the substituent attached to the electrofuge moiety. This contribution closes the set of relationships between philicity and fugality quantities in the sense that while nucleofugality appears related to group electrophilicity of the leaving group, electrofugality is related to the group nucleophilicity of the permanent group.

Supporting Information Available. Cartesian coordinates and energies. This material is available free of charge via the Internet at http://pubs.acs.org.

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