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The size of the alpha-effects in methyl transfers correlate with Koopmans' theorem ionization potentials

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ABSTRACT: The size of the alpha-effects in methyl transfers to the alpha-nucleophile's peroxide anion and two *N*-methylbenzohydroxamate anions correlate strongly with the Koopmans' theorem ionization potentials of the leaving groups. This correlation supports the Shaik and Pross valence bond configuration mixing theory for the S_N2 reaction. The Koopmans' theorem ionization potentials of the alpha-nucleophiles relate to the slopes of the regression plots inversely, indicating that the size of the alpha-effect depends on a balance between the ability of the alpha-nucleophile and the leaving group to donate single electron character to the methyl group. Copyright © 2005 John Wiley & Sons, Ltd.
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KEYWORDS: ionization potentials; S_N2 mechanism; Koopmans theorem; methyl transfers

INTRODUCTION

The alpha-effect refers to an enhanced nucleophilic reactivity possessed by a nucleophile, such as the hydrogen peroxide anion, which has a lone pair of electrons on the atom next to (alpha atom) the nucleophilic atom. Structure **1** shows a stylized alpha-nucleophile.

:X-Y:
1

The enhanced reactivity is often measured on a Brønsted-type plot of log *k* vs the pK_{HA} of several alpha-nucleophiles and normal nucleophiles.[1] The difference between the log *k* values of the two straight lines at a selected pK_{HA} value (for both the alpha- and the normal nucleophiles) gives the size of the alpha effect. The simplest expression of the alpha-effect is, of course, the anti-log transform of this value giving the ratio of rate constants.

The largest expression of the alpha-effect involves nucleophilic attack at the carbonyl[1,2] or other low LUMO substrates, but smaller alpha-effects are found in methyl transfers to peroxide anion from substituted phenyl methyl sulfates[3] and in methyl transfers to *N*-methylbenzohydroxamates (NMBH) from substituted methyl tosylates[4] and aryl methyl sulfides.[5]

Methyl transfers as S_N2-type reactions have been treated in the last 20 years as a valence bond configuration mixing (VBCM) model in which a many-curve modeling of the reaction profile is done.[6] The chief embodiments of the concepts of this mechanism are shown in a state correlation diagram (SCD) as in Fig. 1. The transition state (TS) occurs as an avoided crossing of the reactant Ψ_a and product Ψ_b contributions, modified by inclusion of the two higher contributors. The valence bond total transition state wave function is given in Eqn (1):

$$\Psi^{\ddagger} = a_{\psi_a} + b_{\psi_b} + c_{\psi_c} + d_{\psi_d} \tag{1}$$

The Lewis structure representations are also given in Eqn (1) for conceptual clarity. The contribution from ψ_d indicates the inclusion of any single electron transfer (SET) character in the TS.

The Hoz[2] electronic model of the alpha-effect, Fig. 2, fits the ideas in the VBCM model. This Hoz model originally invoked only low LUMO substrates, but with the finding of small alpha-effects occurred even in methyl transfers in S_N2-type reactions has been applied to help understand the correlations of the size of the alpha-effect on experimental SET-type parameters. Such parameters as reduction potentials[4] of the substrates, oxidation potentials of the alpha-nucleophiles and the Koopmans' theorem ionization potentials (IPs) of the alpha-nucleophiles[4,5,7,8] all correlate rate constants for the alpha-nucleophiles and attest to the possibility of the involvement of such SET transfers in their reactivity.

If such SET character was provided in the TS by the alpha-nucleophiles in methyl transfer, then the mixing coefficient, *d*, in Eqn (1) would be increased, and at least one component of the alpha-effect would be explainable by including the three-electron stability inherent in the Hoz model to lower the energy of the TSs in

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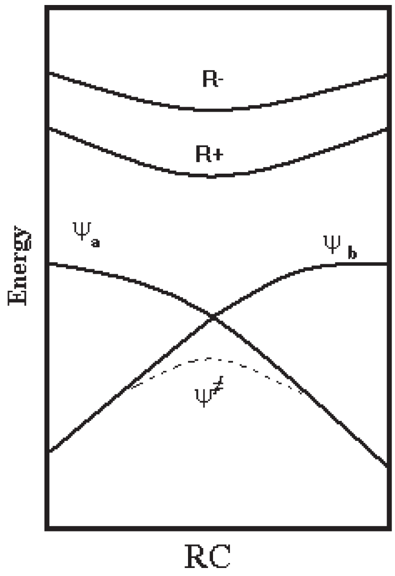


Figure 1. An SCD for a general chemical reaction

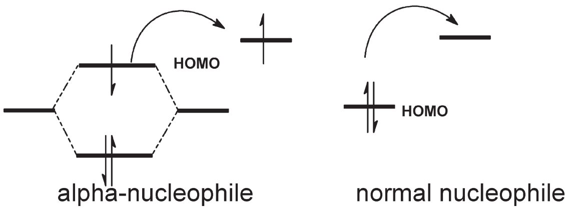
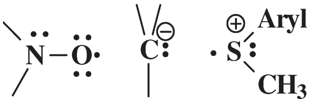


Figure 2. Hoz model for the alpha-effect

alpha-nucleophilic activity. This capacity of the alpha-nucleophiles to donate SET character can be modified by structural variations on the nucleophiles to increase or decrease it,[5] as we have successfully shown, using the tool of increasing electron demand.[5]

A second capacity, to receive SET character, must exist in the leaving group–methyl system, as pointed out previously,[4] for the nucleophile–substrate interaction to show such a SET-dependent alpha-effect. Expressing this capacity involves application of Eqn (1) to particular leaving groups in particular nucleophilic reactions. An example of such particularization is shown in structure **2**, which involves reaction (2).



2

$$\begin{aligned}&\text{Nuc:}^- + \text{Me S}^+{-}(\text{Me})\text{Aryl}^2 \rightarrow \text{Nuc}{-}\text{Me} + \text{MeSAryl}^2\\ &\text{Nuc:}^- = \text{Aryl}^1\text{CON(Me)O}^-\\ &\qquad = \text{Aryl}^3\text{O}^- \end{aligned} \qquad (2)$$

$$\begin{aligned}&\text{Nuc:}^- + \text{MeOSO}_3\text{Aryl}^2 \rightarrow \text{NucMe} + \text{O}^-\text{SO}_3\text{Aryl}{-}\text{X}\\ &\text{Nuc:}^- = \text{HOO}^-, \text{HO}^- \end{aligned} \qquad (3)$$

This particularization of ψ_d in Eqn (1) denotes the mutual donation of the SET character of the nucleophile and the leaving group to the CH_3 group, and suggests that the leaving group's ability for such SET donation will affect an alpha-effect that depends on the SET character of at least some of its expression. This paper deals with evidence that this second capacity for SET character inclusion is realized in correlations of Koopmans' theorem IPs of leaving groups.

EXPERIMENTAL

The preparation of all the compounds, and the experimental data characterizing them and the rate constants for reactions (2) and (3) have been published previously.[3–5,7,8] All of the reactions were run in methanol followed by UV spectroscopy for reaction (3), or by analysis using ^{1}H NMR in methanol-d_4 for reaction (2). The alpha-effects, expressed as $\log k_{\text{alpha}} - \log k_{\text{normal}}$, have been reported previously, but are collected in Table 1 for ease of discussion here.

Computational chemistry for the substituted methyl aryl sulfide leaving groups in reaction (2) and the substituted phenylsulfate leaving groups in reaction (3) was performed by first drawing the leaving group structures in the GUI of Hyperchem 6.02 (HyperCube, Gainesville, FL, USA) and optimizing the structures at the PM3 level of theory. Optimization of the PM3 level structures was subsequently done at the RHF/6–31G* level, then done using Gaussian 98W or Gaussian 03W.[9] Visualizations of the completed jobs were obtained by GaussView 03 (Gaussian, Pittsburgh, PA, USA). Frequency calculations revealed that satisfactory minima were obtained. The

Table 1. Correlations of alpha-effects with Koopmans' theorem IPs for leaving groups

Leaving Groups	X or Aryl	Alpha-nucleophile	Alpha-effect[a]	IP (eV)[b]
$XC_6H_4OSO_3^-$	*m*-NO_2	HOO^-	0.756	6.008
	p-Br		0.898	5.435
	H		1.041	5.160
	p-Me		0.996	4.999
XC_6H_4SMe	H	$NMBH^-$ [c]	2.210	8.021
	p-NO_2		1.937	8.889
	p-CN		1.874	8.622
	p-Me		2.593	7.834
	p-Cl		1.937[d]	8.214
MeSAryl	Phenyl	*p*-ClNMBH[e]	1.124	8.021
	1-Naphthyl		1.512	7.441
	9-Anthracenyl		1.835	7.116
	DBT[f]		1.137	7.950

[a] Defined as $\log k_{\text{alpha}} - \log k_{\text{normal}}$.
[b] Computed at the RHF/6–31G* level from a completely optimized geometry.
[c] $C_6H_5CON(Me)O^-$.
[d] Interpolated from the data in Ref. 5.
[e] 4-$ClC_6H_4CON(Me)O^-$.
[f] Dibenzothiophene.

Koopmans' theorems IPs were extracted as the negative of the HOMO[10] orbitals in each case. These values are likewise summarized in Table 1, and plotted in Fig. 3.

Koopmans' theorem IPs at a sufficiently high level of theory are sufficient to give approximate IPs because when using an HF model theory fortuitous cancellation of errors occurs. The orbital relaxation (redistribution of electrons within the entity remaining after removal of the electron) and the electron correlation effects offset one another. In practice, this offsetting is often within 0.3 eV of the experimental values. In the present cases the trends in IPs through such series should be suitably represented at the RHF/6–31 G* level (usually required for an error of 0.3 eV). Comparing some known experimental IP values makes this case sound in this research. The reported experimental IP of thioanisole is 8.07 eV,[11] indicating excellent agreement with the RHF/6–31G* value (8.021 eV) in Table 1. A test computation of thioanisole at the RHF/6–31+G* level of theory disclosed an IP value of 8.15 eV, a value insignificantly different from that at the RHF/6–31G* level.

For the substituted phenylsulfates where experimental IPs are not yet known, nor are those for the related substituted benzenesulfates known, a similar test of the effects of a higher level of theory gave at the RHF/6–31+G* level an IP of 5.48 eV vs the 5.23 eV value in Table 1. This result indicated that the lower level of theory, RHF/6–31G*, would be suitable for the IPs in the substituted phenylsulfate anion series.

RESULTS

The regressions in Fig. 3 indicate that the dependence of the alpha-effect on the ability of the leaving group to contribute SET character via ψ_d in Eqn (1) depends also on the alpha-nucleophiles, as expected. The putatively strongest alpha-nucleophile,[1] HOO^-, has the smallest dependence on the leaving groups' ability, as shown by the smallest slope (−0.272). The other two alpha-nucleophiles likewise exhibit this trend as follows. The more basic NMBH ($pK_{HA} = 12.384$) gives the larger alpha-effect and less dependence on the leaving groups' IPs (slope = −0.654), whereas the less basic 4-ClNMBH ($pK_{HA} = 12.04^4$) gives less alpha-effect, with more dependence on the leaving groups IPs.

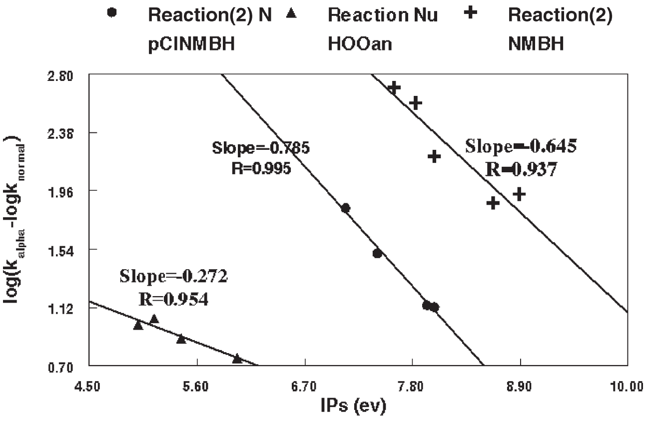


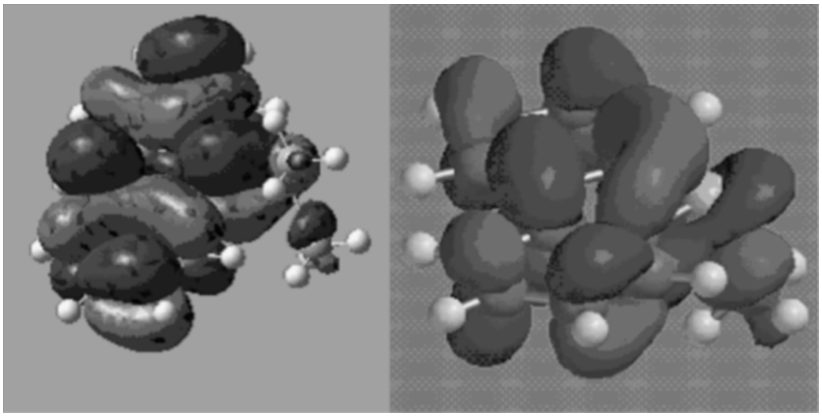
Figure 3. Correlation of alpha-effects with leaving group IPs

DISCUSSION

If the alpha-effects depend on the ability to transfer SET character of the alpha-nucleophiles, one would predict that some experimental parameter, reflecting SET character, such as an oxidation potential, would correctly order the three alpha-nucleophiles in Table 1. The experimental oxidation potentials of the substituted NMBH anions (GNMBH) correlate the k_{nuc} values strongly[4] (slope = 1.065[7] in consistent units of energy) in methyl transfers to substituted NMBH anions from 4-methoxybenzenesulfonate at 30 °C in MeOH. A very similar correlation (slope = 1.061) was found for methyl transfers to GNMBH anions from methyl aryl sulfides.[5] Comparing $E_{1/2}$ (oxidation potential) values for NMBH and 4-ClNMBH anions gives 165.0 vs 175.1 mV (interpolated from data in Ref. 4) (both in MeOH), indicating that NMBH is a better SET donor under solution conditions. A similar correlation occurs in alpha-nucleophile-organic cation combination reactions.[12] The slopes in Fig. 3 for the two NMBH anion lines indicate that the better SET donor in reaction (2) has less dependence on the SET donated by the leaving group. The oxidation potential of peroxide anion in MeOH is not available.

Gas-phase SET behavior can be modeled by Koopmans' theorem IPs. In this way all three reactions can be evaluated in the gas phase. The IP values are $HOO^- = 1.83$ eV (RHF/6–31G* level of theory), 4-ClNMBH anion = 3.025 eV (RHF/6–31G* level) and NMBH anion = 2.774 eV (RHF/6–31G* level). These gas-phase IPs also are consistent with the concept that the stronger alpha-nucleophile, peroxide anion, gives less dependence of the alpha-effect on the leaving group's ability to donate SET character to the C atom.

It is important to note that reduction potentials of the aryldialkylsulfonium cations in reaction (2) do not correlate all the members of the series presented in Table 1, but the Koopmans' theorem IPs of the leaving groups do. This fact deserves explanation. Electrochemical reduction of the aryldialkylsulfonium cations where aryl = phenyl, 1-naphthyl, and 9-anthracenyl are reported to involve insertions of single electrons into a LUMO involving mostly the CH_3—S bond as a σ^* orbital (at the AM1 level of theory),[13] which is at a lower energy than the perturbed aryl π^* molecular orbital. The σ^* and π^* in that report were deemed to be separate entities, and also apparently in the systematic study of these species by Andrieux *et al.*[14] In that paper, the standard potential for injection of one electron into 9-anthracenyldimethylsulfonium cation was considerably positive by 600 mV



Scheme 1. LUMOs of 9-anthracenyldimethylsulfonium and *S*-methyldibenzothiophenium cations

compared with anthracene. This fact was interpreted as indicating a strong interaction between the π^* orbital of the anthracenyl group and the orbitals of the sulfur atom. Putatively the injection of a single electron into an aryldialkylsulfonium system involves the π^* system.[15] However, electrochemical evidence[15] provided a conclusion consistent with a concerted σ sulfur–carbon bond breaking concomitant with electron acceptance.[16] A refinement of this conclusion in Ref. 16 was stated, namely that passage from a stepwise ET process (injection of a single electron followed by dissociation of a radical from the sulfuranyl radical) to a concerted process, wherein radical departure concomitant with one-electron acceptance was dependent on molecular structure.[14]

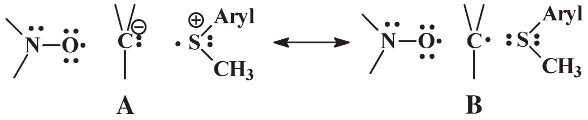
Some insight into the details of the electronic structure of these sulfonium cation systems is obvious from the presentation of the RHF 6–31G* level MOs of the 9-anthracenyl and methyl-DBT cases in Scheme 1. As can be seen, the LUMOs of these cations consist of both σ^* and π^* components. Considerable delocalization into the π^* component exists. This complicates the explanation of the SET character donated by these kinds of leaving groups. Certainly, from the nucleophile side the entry of SET character to the C atom is supported by the injection of one electron into the S—CH$_3$ σ^* component of the LUMO. The explanation of this support is relatively straightforward, as follows.

The Hoz model, as in Fig. 2, for SET character is supported by the reports of stability of three-electron anionic bonds by Hiberty.[17–21] The original concept reported by Hoz included this idea.[2] Inclusion of this additional stability into the TS for the alpha-effect would lower the activation energy experienced by the TS. Application of the three-electron concept for leaving groups, as required by Eqn (1), requires some subtle modifications as in the next few paragraphs.

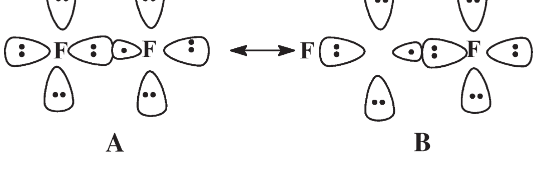
First, the particular representations of ψ_d for the methyl aryl sulfide leaving groups, as in Scheme 2, must take into account the stabilization energy supplied by this contribution. This can be properly done with the concept of Breathing Orbitals in the valence bond theory (BOVB), as reported by Hiberty.[17–21] This BOVB concept is illustrated in Scheme 3, using Hiberty's own example (numbers and letters of structures are as in Hiberty[19]). From this simple modification of VB concepts they were able to compute the correct dissociation energies for several three- electron bond radical anions, indicating the level of its validity. A stated conclusion of the BOVB method is that the orbital possessing a pair of electrons would have an expanded volume compared with the orbital having only one electron. The resonance implied in Scheme 3 provides the additional stability.

The different sizes of the singly occupied AOs and doubly occupied AOs are indicated in Scheme 3. When this idea is applied in a heteroatomic bond, the implication is that the atom most able to support the large orbital makes the canonical structure including that atom the more important one (i.e. the more stable canonical structure).

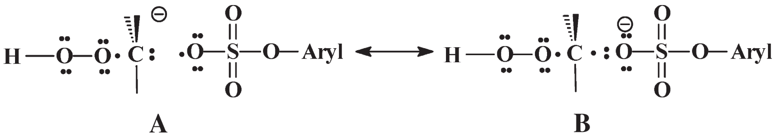
Application of these concepts to the transition states of the reactions (2) and (3) gives particular representations for ψ_d in Schemes 2 and 4. Note that the lone pair of electrons in contributor **B** in Scheme 2 resides in the orbital next to the π orbital system of the aryl ring—the potentially larger MO. At the RHF/6–31G* level of theory, the HOMOs of a leaving group such as PhSMe shows extensive delocalization throughout the aryl system, and into the methyl group, whereas the $PhOSO_3^-$ [22] system at the same level of theory shows



Scheme 2. Three-electron bond resonance for reaction (2)



Scheme 3. Three-electron bond resonance for the F$_2$ anion



Scheme 4. Three-electron bond resonance for reaction (3)

less delocalization of charge on or near the SO_3 portion of the anion. These MOs are supplied in the Supplementary material (available in Wiley Interscience).

An argument can be made from these two different kinds of orbital systems that the pair of electrons in contributor **B** in Scheme 2 would be more stable than contributor **B** in Scheme 4, thus making the IPs larger than in the phenylsulfate leaving group, and thus stronger dependence on this parameter for expression of any alpha-effect which depends on SET character for its expression.

CONCLUSIONS

The correlations of the Koopmans' theorem IPs of both the alpha-nucleophile and the leaving groups with the size of the alpha-effects in these methyl transfers supports the concept that the alpha-effect in methyl transfers involves some SET character. The different slopes of the IP correlations of differing strength alpha-nucleophiles indicate a balance of SET character between the alpha-nucleophile and the leaving groups. If the alpha-nucleophile is better at donating SET character, less donation of SET character is demanded of the leaving group. Taken together, these results strongly reinforce the concepts expressed in the SCD model, and Eqn (1) for the S_N2 reaction and the Hoz model for the alpha-effect.

Supplementary material

Visual HOMOs of thioanisole and phenylsulfate anion, and Gaussian job files, suitable for single point computation of the output files, for all the leaving groups, are available in Wiley Interscience.

Acknowledgments

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