

The Alpha-Effect. A Theoretical Study Incorporating Solvent Effects

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Several recent studies have shown that OOH^- has no greater reactivity than OH^- in the gas phase. This is in striking contrast to the solution phase observation that OOH^- has an enhanced nucleophilicity over OH^- (the "alpha-effect"). The gas-phase results were thought to put into jeopardy the FMO orbital-splitting explanation of the alpha-effect, since, it was reasoned, such an effect should be independent of solvent. However, the calculations reported here, based on MINDO/3 and solvaton theory (to take account of the effects of solvent), show that the extrapolation of the gas-phase results to solution is invalid and that orbital-splitting does play an important role in the enhanced nucleophilicity of OOH^- over OH^- in solution.

INTRODUCTION

Recent studies^{1,2} have established that the "alpha-effect", *i. e.*, the enhanced nucleophilicity of alpha-nucleophiles³ observed in some solution reactions is not observed in the corresponding gas phase reactions.

The general alpha-effect manifests itself by an increased nucleophilicity, as defined by a positive deviation from the Bronsted equation (Eq. (1)), which is based on the more general Bell-Evans-Polanyi (BEP) principle⁴:

$$\log k = C + \alpha pK_b \quad (1)$$

where k is the rate constant and pK_b is the negative log of the basic equilibrium constant. It is observed when a heteroatom is located in the position alpha to the reacting atom of a nucleophile³. The classical example is that observed by Jencks and Carriulo⁵ in the reaction of a series of nucleophiles with *p*-nitrophenyl acetate in aqueous solution. They found that OOH^- reacted by several orders of magnitude faster than OH^- with *p*-nitrophenyl acetate, and this, in spite of the fact that OH^- is much more basic. A more recent example involves a comparison between OOH^- and MeO^- .⁶ Here again, a tenfold difference in rate was observed in favor of OOH^- for an SN_2 displacement reaction on methyl phenylsulfates.

Explanations for the alpha-effect have mostly followed two trains of thought: 1) the alpha-nucleophile (for example, OOH^-), is less solvated and therefore more reactive,⁷ than, say, hydroxide ion or 2) overlap between the adjacent π orbitals results in an increase in energy of the highest occupied

molecular orbital (HOMO) of the alpha-nucleophile.⁸ Then, according to frontier molecular orbital (FMO) theory,⁹ in an orbital-controlled reaction,^{8a} the highest reactivity is to be observed for that species in which the HOMO of the nucleophile is closest in energy to the lowest unoccupied molecular orbital (LUMO) of the electrophile.

This means that the species with the highest HOMO energy has the highest reactivity. In this instance, the highest energy had always been assumed to be that of the HOMO of alpha-nucleophile, *i. e.* OOH^- .^{8b} However, the recent *ab initio* calculations of Wolfe² have indicated that this is not true; indeed, the HOMO of OOH^- was found to be lower in energy than that of OH^- . This lowering of the OOH^- HOMO energy, which was attributed to the high electronegativity of the alpha-oxygen atom agrees with the experimental observation that OOH^- is not more reactive than OH^- in the gas phase,¹ but also throws into doubt the FMO explanation of the observed differences of reactivity in solution.

The gas-phase results were also thought to contradict the FMO orbital-splitting explanation of the alpha-effect, since, it was reasoned, such an effect should be independent of solvent. We have recently carried out some calculations incorporating the effects of solvent that we believe may have some bearing on the question.

METHOD

Theoretical methods capable of evaluating the effects of solvent, have been under development for several years, but have not yet reached the point of wide utilization.¹⁰ Our laboratory, though, has been working on such a method for the past several years, utilizing the solvaton¹¹ theory which, coupled with the MINDO/3 methodology, gave the MINDOS program.¹² Applications of the solvaton theory have been reported by other authors and have proven useful in predicting the effect of solvent on such molecular properties as total energy, electronic transition energies and spin densities of radical anions.¹³

Our own extensions have found use in successfully modelling aqueous dissociations of a number of hydride species.¹² The latest version of MINDOS also incorporates a correction to gas-phase energies, in particular, of anions.¹⁴ Indeed, energies of anions are notoriously poorly reproduced by almost all theoretical methods including the 4-31G method used by Wolfe. The only exceptions are those methods carried out at the Hartree-Fock limit.¹⁵ This may not present problems where the same bond-forming reaction is compared, but still casts some doubt on any conclusions drawn from such calculations. The current approach to the alpha-effect consisted of applying the MINDOS method to model the effect of solvent (water) on the thermodynamic properties and orbital energies of the OH^- and OOH^- ions.

RESULTS AND DISCUSSION

The results are presented in Tables I and II. The MINDOS method is a semi-empirical method and as such is parametrized. While thermodynamic quantities associated with OH^- were included in the parametrization, those of OOH^- were not. In spite of that, it can be seen that the enthalpies of formation for both species, in the gas and the solvent phase, do compare well

TABLE I

Comparison of Gas Phase and Solvent (Water) Phase Enthalpies of OH^- , OOH^- and H_2O^a

	$\Delta H_{f(g)}$		$\Delta H_{f(s)}$		ΔH_{aq}	
	MINDOS	Exp.	MINDOS	Exp.	MINDOS	Exp.
HOH	-57.5	-57.8 ^b	-68.0	-68.3 ^b	-10.5	-10.5 ^b
HOOH	-38.8	-32.6 ^b	-52.7	-45.7 ^b	-13.9	-13.1 ^b
HO^-	-35.2	-33.7 ^b	-55.1	-55.0 ^b	-19.9	-21.3 ^b
HOO^-	-37.3	-24.9 ^c	-43.6	-38.3 ^b	-6.3	-13.4 ^c
Difference in ΔH_{aq} [OH^-]- OOH^-]					-13.6	-7.9 ^c

^a Dimensions are kcal/mol; conventions of Note b. adopted, specifically, the enthalpy of formation of $\text{H} + (\text{aq})$ is assigned the value 0;

^b From reference 16;

^c From reference 17.

TABLE II

Comparison of Gas Phase and Solvent Phase HOMO Energies for OH^- and OOH^- as Calculated by MINDOS^a

	Gas	Solvent
OH^-	-2.28 (-0.93) ^b	-12.50
OOH^-	-1.80 (-2.36) ^b	-9.64
difference	-0.48 (1.43)	- 2.86

^a Energy units are eV;

^b From Wolfe, reference 2.

with experimental quantities. It is of special interest to note that the calculated difference in enthalpy of solvation between OH^- and OOH^- is close to the value obtained from a standard compilation¹⁶ of heats of formation and the new experimental heat of formation in the gas phase for OOH^- recently reported by Lineberger, *et al.*¹⁷. Column 2 of Tables I and II show the heats of formation and HOMO energies of OH^- and OOH^- in the gas phase. Even though the HOMO's of the two species in this phase do not parallel the *ab initio* results of Wolfe,² in that the HOMO of OOH^- is calculated to be higher than that of OH^- , this difference is small and therefore consistent with the experimental finding that, in the gas-phase, there is little reactivity difference between OH^- and OOH^- .¹ In solution, though, the calculations show that the orbitals of OH^- are more stabilized by the transfer to this phase than are those of OOH^- , and, as a consequence, the HOMO of the hydroxide ion drops substantially below that of OOH^- . Figure 1 illustrates this situation as well as the hypothetical case that would have been observed if there was no interaction between the adjacent orbitals of the alpha-nucleophile (dotted line). It can be seen that, in the latter case, not only is the solvation energy difference between the two species significantly decreased, but, because the HOMO

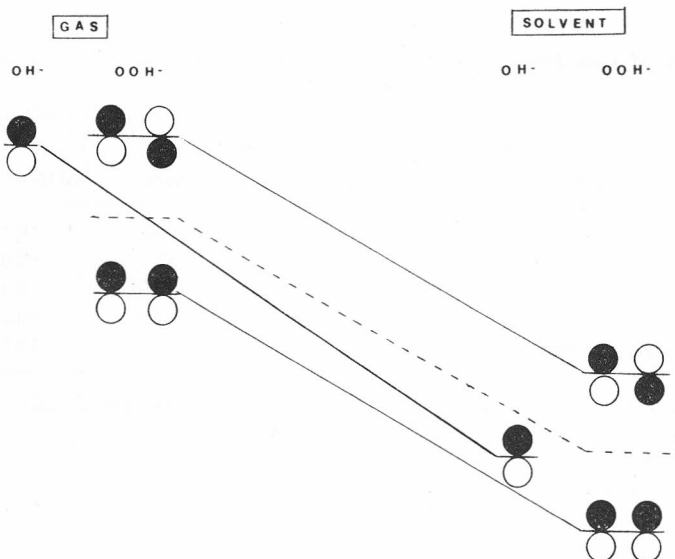


Figure 1. Correlation diagram showing the effect of solvent on the HOMO of OH^- and the in-phase and out-of-phase combinations of p -orbitals on OOH^- (including its HOMO). The dotted line represents the assumed correlation for the degenerate level of OOH^- in the absence of splitting.

energy would not now be significantly higher than that of the OH^- , the FMO theory would predict little difference in reactivity even in solution.

What this shows is that the solvation explanation is not independent of the lone-pair interaction explanation for the increased reactivity of α -nucleophiles. Rather, the two effects work in concert to produce the phenomenon known as the α -effect. However, that is not to say that the explanations are equivalent. For instance, it is not clear that "solvation" as generally meant in the literature can successfully explain the effect of a change in electrophile. This was discussed in some detail in an earlier paper.^{8b} In one such case, *p*-nitrophenyl acetate was found to react 300 times more rapidly with OOH^- than OH^- .⁵ On the other hand, ethyl acetate reacted some 10,000 times less rapidly with OOH^- than with OH^- .¹⁸ Clearly, if differential solvation of the two nucleophiles was the most important factor in the α -effect, then OOH^- should have similar relative reactivities in each example. As we have shown previously,^{8b} the reactions of ethyl acetate with OH^- and OOH^- are examples of charge-controlled reactions, while the reactions with *p*-nitrophenyl acetate are "frontier-orbital" controlled.^{8a} As such, orbital-splitting is a crucial factor in the latter reaction, but not so important in the former.

The calculational results presented, based on the semi-empirical MINDOS method, support the lone-pair repulsion explanation of the α -effect.⁸ It is important that the α -effect not be explained away as a vague "solvent" effect. The α -effect still represents an exception to the generally successful

and useful BEP principle,⁴ and, as such, it is important to chart the reasons for its exception in detail so that new exceptions may be anticipated.

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SAŽETAK

Alfa-efekt. Teorijski studij s pomoću MINDO/3 metode i teorije solvatacije

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Rezultati nekih nedavnih istraživanja pokazuju da anioni OOH^- i OH^- imaju jednaku reaktivnost u plinskoj fazi. To je u direktnoj suprotnosti s eksperimentalnim mjerenjima koja nedvosmisleno potvrđuju da anion OOH^- ima daleko izrazitiji nukleofilni karakter u otopini (tzv. α -efekt). Budući da se pretpostavljalo da α -efekt ne ovisi o otapalu, rezultati za plinsku fazu doveli su u pitanje njegovu interpretaciju s pomoću graničnih molekularnih orbitala (FMO). U ovom radu pokazano je da se α -efekt može objasniti modelom FMO. Utvrđeno je, naime, da cijepanje energijskih razina FMO bitno ovisi o otapalu. Na taj se način FMO-modelom dobiva rezultat koji je potpuno u skladu s empirijski utvrđenom povećanom nukleofilnošću aniona OOH^- .