Can We Predict Reactivity Using MO Calculations?

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Molecular orbital calculations can, in principle, provide extensive information about the course, kinetics, and thermodynamics of chemical reactions. In practice, a full calculation of the kinetics of a simple hydrogen transfer reaction requires calculation of the force constant matrix at high levels of theory at several points along the reaction coordinate and delivers results that are not yet of useful accuracy. Far more promising, however, is the use of molecular orbital calculations to investigate, for instance, the effect of metal ion catalysis on simple reactions. This is demonstrated by ab initio calculations on the activation of $^3O_2$ by complexation with metal ions.

Molecular orbital calculations, either of the semiempirical[1] or of the ab initio[2] type, provide intimate details of the courses of chemical reactions. No other methods, either experimental or theoretical, are capable of providing as much detailed information about the microscopic changes that occur during chemical reactions. It is therefore tempting to try to use molecular orbital theory to predict chemical reactivity. The best known and most widely accepted procedure is to use perturbational molecular orbital (PMO) theory[3] to predict reactivity based on the electronic properties of the starting materials. This works well in some cases, but because the perturbational treatment is based on the electronic properties of the unperturbed starting materials, such a process can only be successful for kinetically controlled processes in which the transition state occurs early in the reaction (i.e., it is close in structure to the reactants). Molecular dynamics (MD) calculations appear to offer an alternative to such perturbational approaches, but require a knowledge of the potential energy hypersurface for the reaction. The first step in most MD investigations of chemical reactions is therefore to calculate the potential energy hypersurface (or the relevant part of it) using MO theory.[4]

The prediction of reactivity by explicit calculation of the course of the reaction (usually by calculation of the stationary points along the reaction path) is, in principle, a far more promising approach. However, exactly as it is impossible to be sure that a given equilibrium structure is the global (most stable) minimum for a given molecular formula, it is impossible to be sure that a calculated reaction path is the most favorable for a given molecule or pair of molecules. The problem in "real" systems is even more complicated because reactions involving solvent, acids, bases, or other components of the reaction mixture may also be more favorable than the required reaction. In practice, molecular orbital theory cannot be expected to predict the kinetics of a given reaction reliably, as will be shown below, but it can provide useful insights into catalytic processes and into the details of a given reaction. At present, this type of approach is best suited to mechanistic studies of known reactions, but some attempts to predict enhanced reactivity for some oxidations by triplet dioxygen ($^3O_2$) will be given below.

A SIMPLE REACTION: $CH_3\cdot + CH_4 \rightarrow CH_4 + CH_3\cdot$

Radical reactions, such as the simple hydrogen-atom transfer shown above, play an important role in many industrial processes and synthetic organic applications. They generally have lower activation energies than equivalent closed-shell reactions

and can therefore be carried out under milder conditions. Atom transfer reactions are often the chain-carrying steps in radical chain reactions, so that a reliable theoretical method to predict their kinetics would be of great value. Unfortunately, the MO methods that are commonly used to calculate open-shell species generally overestimate activation energies, so that these simple reactions are often very difficult to treat theoretically. The calculated (MP2/6-31G*) transition state for the hydrogen-atom exchange reaction between methane and the methyl radical is shown.


(1)
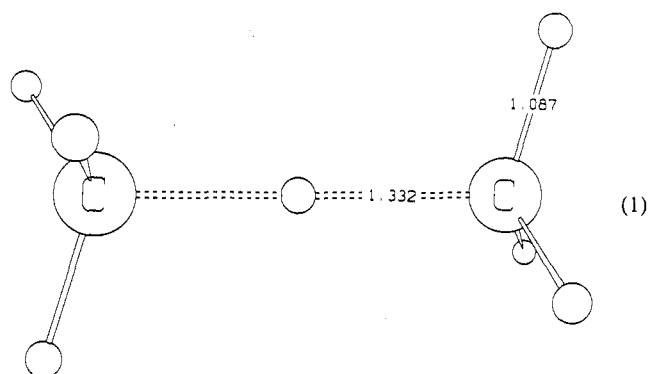
Normally, this level of theory, which uses a moderately large basis set and includes a perturbational correction for electron correlation, would be expected to provide reliable activation energies for closed-shell reactions. For open-shell transition states, however, the unrestricted Hartree–Fock (UHF) wavefunction that is used as a reference wavefunction for the perturbational correlation correction is often contaminated by higher spin states. This spin contamination leads to a significant underestimation of the correlation correction for the transition state and hence to calculated activation energies that are too high. The hydrogen transfer reaction shown in eq 1 is even more difficult because a large part of the reaction occurs by quantum mechanical tunneling. This can be taken into account if the force-constant matrices for a series of points along the reaction path are calculated, and these data are used to calculate the reaction rate using a program, such as Truhlar's POLYRATE, that calculates rate constants based on transition-state theory and semiclassical approximations for tunneling and nonclassical reflection.[5] The basic problem with the height of the reaction barrier remains, however, as can be seen from the calculated data shown in Table I.

The calculated tunneling probabilities for the ^1H reaction range from 100% up at 170K to 22% at 1273K. Apart from

Table I. Calculated (MP2/6-31G*) Activation Energies for Hydrogen-Atom Transfer Reactions

	activation energy (kcal mol^{-1})				
	classical ΔE		polyrate ΔE		exp[6]
reaction	UHF	MP2	$T = 69K$	$T = 298K$	$T = 473-623K$
CH$_3$' + CH$_4$ → CH$_4$ + CH$_3$'	30.2	19.2	9.2	18.7	14.7
CH$_3$' + CH$_3$D → CH$_3$D + CH$_3$'	31.1	20.1	7.9	19.0	
CD$_3$' + CD$_4$ → CD$_4$ + CD$_3$'	30.3	19.3	9.5	19.2	17.8
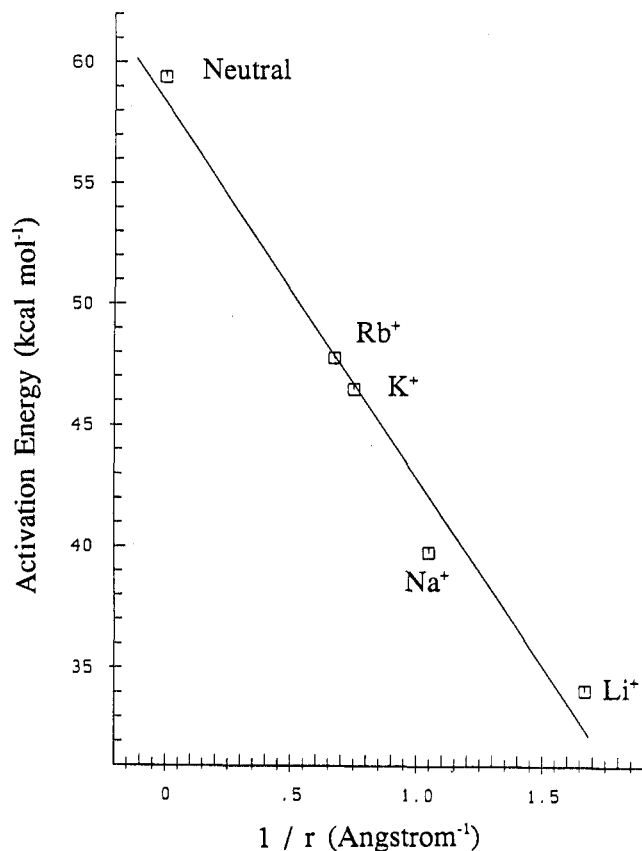
Figure 1. Plot of the calculated activation energies (kcal mol^{-1}) for the reaction of M$^+$:^{3}O with CH$_4$.

the difficulties in calculating the classical motionless activation energy, there also appears to be problems for the rate and significance of tunneling, especially when hydrogen is compared with deuterium. It can be concluded that the ab initio calculation of realistic rate constants is at present unrealistic for reasonably sized reactions.

ACTIVATION OF TRIPLET DIOXYGEN

Triplet dioxygen, ^{3}O$_2$, is chemically remarkably inert. Its activation in biological or industrial reactions has been the subject of a great deal of research. Because of the similarity between triplet and radical reactions, it appeared likely that we should be able to extend the principles that led to the investigation of metal-ion catalyzed radical reactions[7] to the catalysis of oxidations by ^{3}O$_2$. As a first example, we investigated hydrogen-atom abstraction from menthane by ^{3}O$_2$.

$$^3O_2 + CH_4 \rightarrow HOO\cdot + CH_3\cdot^8$$
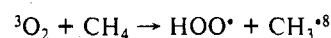
The reaction of ^{3}O$_2$ with methane is endothermic by about 55 kcal mol^{-1}. Nevertheless, this reaction plays an important role in combustion processes and is the prototype for biological autoxidation reactions in which ^{3}O$_2$ abstracts a hydrogen atom from activated C–H donor positions. The calculated activation energy (UMP4sdtq/6-31G*//6-31G*) for the unperturbed reaction is 59.4 kcal mol^{-1}. The oxygen can, however, be complexed to alkali metal cations. This complexation results in a strong charge and spin polarization of the ^{3}O$_2$ moiety and hence to enhanced reactivity. There is also a major thermodynamic effect that results from the fact that the complexation

Scheme I. Course of the Hydrogen Abstraction from Methane by M$^+$: ^{3}O$_2$, Bond Lengths Shown are for M = Li
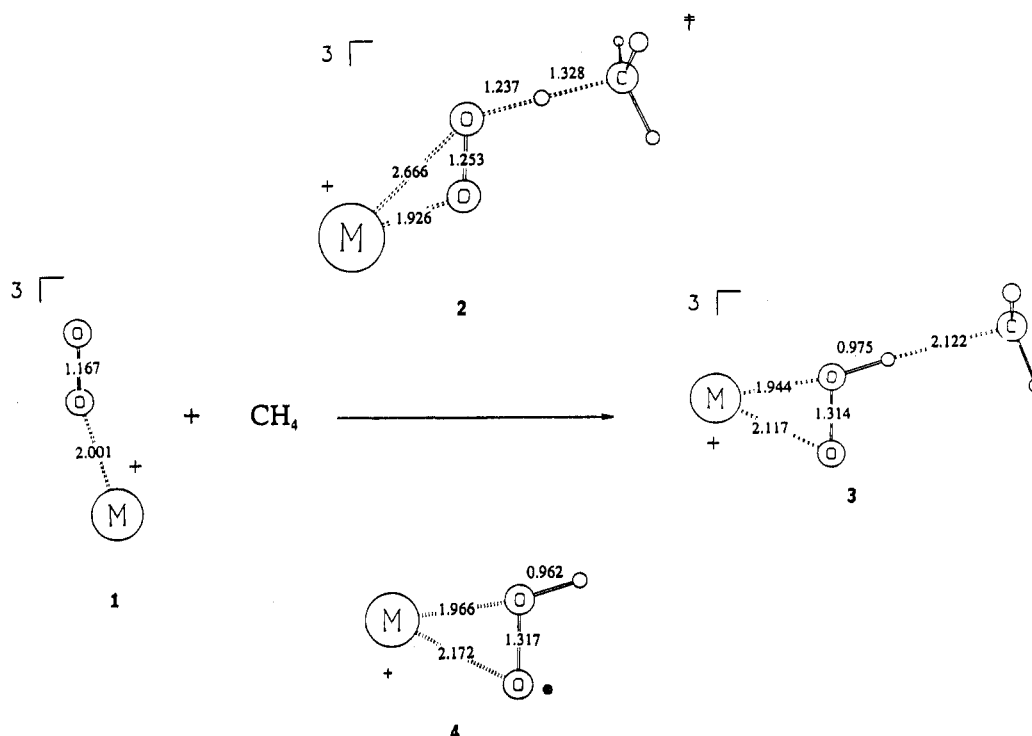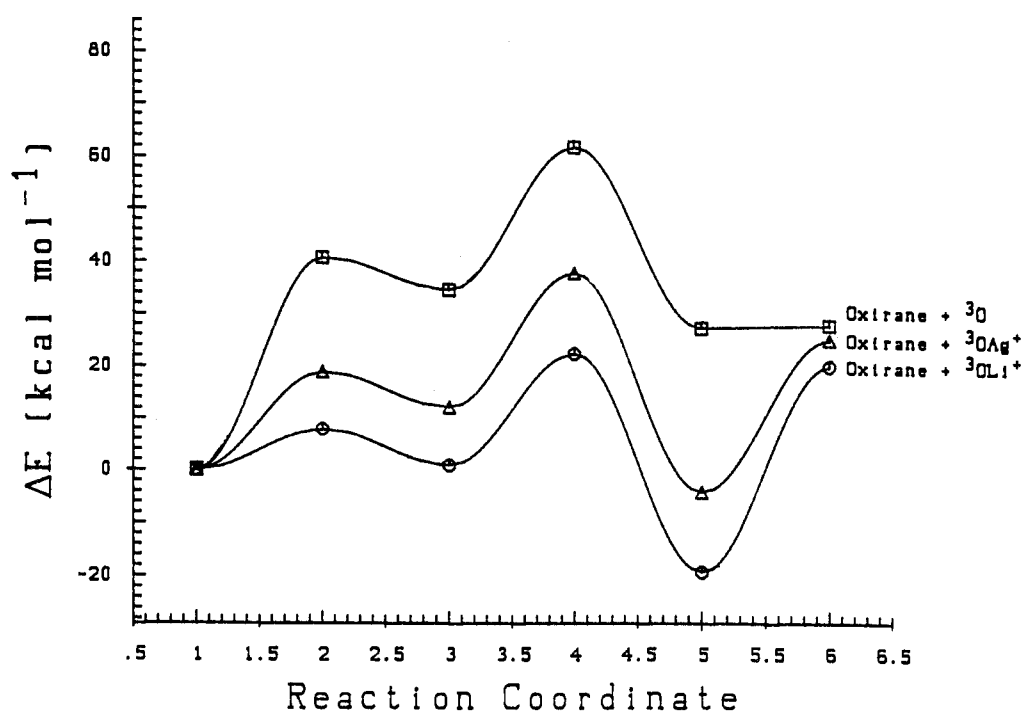
Figure 2. Schematic reaction profiles for the reaction of $^3O_2$ (above), $Li^+:^3O_2$ (below), and $Ag^+:^3O_2$ (center) with ethylene to give oxirane.

Chart I

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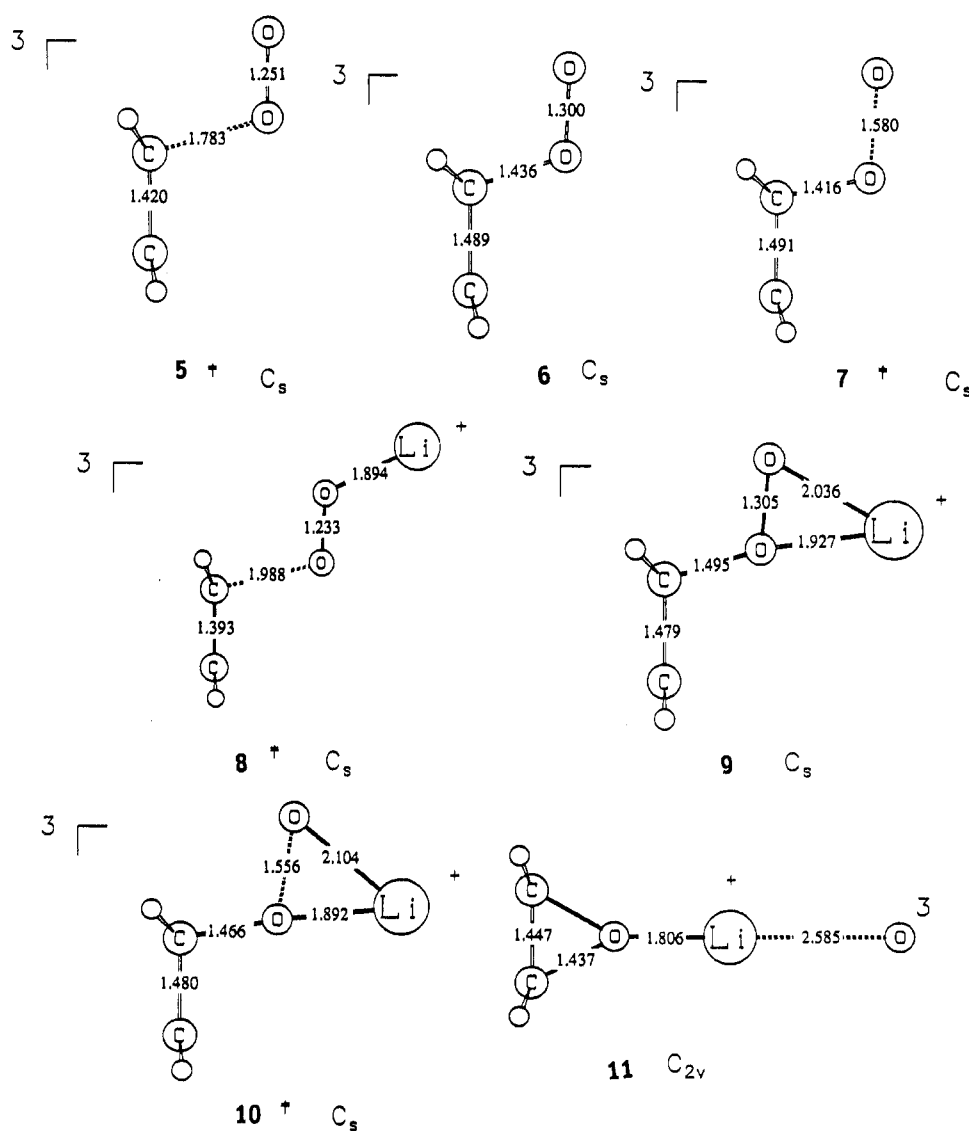
energies between the alkali metal cations and dioxygen species increase strongly in the order $^3O_2 <$ ROO$^\bullet <$ ROOR' (R and R' = H, alkyl, or aryl). This effect is also largely electrostatic in nature and results from the favorable $R^{\delta+}-O^{\delta-}-M^+$ polarization in the reduced oxygen complexes. Calculation of the reaction of $M^+:^3O_2$ complexes with CH_4 gives structures of the type shown in Scheme I (the geometries are given for the Li$^+$ complex). The calculated activation energies for M = Li, Na, K, and Rb are 35.2, 39.9, 46.5, and 47.8 kcal mol^{-1}, respectively. The Li$^-$ and Na$^+$-catalyzed reactions occur without excess activation energy (i.e., the back-reaction occurs without a barrier), and the transition states for K and Rb lie 0.9 and 0.8 kcal mol^{-1}, respectively, above the energies of the products. Strong thermodynamic and kinetic effects therefore favor the hydrogen abstraction by triplet dioxygen. Similar effects are known for transition metal complexes with $^3O_2$, especially for cytochrome P450, but our studies have shown that the catalysis is largely electrostatic in nature. To illustrate this point, Figure 1 shows a plot of the calculated activation energies for the five oxidation reactions vs the reciprocal of the ionic radii of the alkali metals. The two quantities are clearly related, even if the straight line should not be taken too seriously.

EPOXIDATION OF ETHYLENE BY $^3O_2{}^9$

Another important reaction of $^3O_2$ is the epoxidation of olefins. The uncatalyzed reaction is calculated to occur in two steps. First, the $^3O_2$ adds to the ethylene via transition-state **5** (see Chart I) to give the triplet dimethylene peroxy diradical **6**. This reaction is calculated to be endothermic by 34.4 kcal mol^{-1} and to have an activation energy of 40.6 kcal mol^{-1}. The second step is the concurrent cleavage of the O–O bond and the oxirane ring closure. This reaction occurs via transition state **7** with an inactivation energy of 27.2 kcal mol^{-1} relative of **6**. The entire reaction $^3O_2 + C_2H_4 \rightarrow$ oxirane + ^3O is calculated to be endothermic by 27.7 kcal mol^{-1}.

The Li$^+$-catalyzed reaction occurs similarly. The Li$^+:^3O_2$ complex **4** reacts with ethylene via transition state **8** to give the triplet peroxy complex **9** with an activation energy of only 7.8 kcal mol^{-1} in a reaction that is essentially thermoneutral. Once again, both the thermodynamic and the kinetic effects of alkali metal complexation to $^3O_2$ are operative. The second step in the Li$^+$-complexed reaction is not as strongly catalyzed as the first, but there is nevertheless a significant effect. The O–O bond-cleavage/ring-closure transition state **10** lies 21.5 kcal mol^{-1} higher in energy than **9** and the reaction leads to

the complex **11**, which is calculated to be 19.3 kcal mol^{-1} more stable than the starting materials. Figure 2 shows the two reaction profiles schematically and also shows the Ag$^+$-catalyzed reaction profile. The transition metal also catalyzes the reaction, but not as effectively as the smaller alkali metal. Once again, the catalysis appears to be largely electrostatic in nature.

CONCLUSIONS

Molecular orbital theory is not yet able to provide accurate reaction kinetics, even for ground-state gas-phase reactions, but can be extremely useful for mechanistic studies or for investigations designed to compare an unperturbed reaction with its catalyzed counterpart. The major difficulty that remains is to be able to guarantee that the calculated reaction path is the most favorable one open to the system, but this is likely to remain a matter for chemical intuition. The metal ion catalyzed reactions shown above, for instance, are unlikely to be observed under real conditions because the $M^+:^3O_2$ complexes are too weakly bound, but they serve as admirable models for more complicated s Investigation of these more complex systems (or at least models of the active sites) can be performed using semiempirical MO theory and confirms the similarities between the "naked" ions and their more realistic counterparts.ystems such as zeolites and enzymes, in which a favorable coordination site for the substrate on a suitable metal can be guaranteed.

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