

Stereochemistry and Regiochemistry in Model Electron Transfer and Substitution Reactions of a Radical Anion with an Alkyl Halide

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It is common wisdom that transition states (TS's) for polar organic reactions follow a maximum overlap principle. Less well established, however, are the bonding principles that govern the structure of electron transfer (ET) TS's.¹ In this respect, the outer-sphere (weak-bonding) notion provides a powerful ET paradigm,² but one that lacks the structural aspect, while the inner-sphere notion is akin to structural thinking and should follow some definite bonding principles. When does the ET-TS become inner-sphere, and what would then be its bonding principles? Are the bonding principles different for ET and polar TS's,³ and in which respect? These are the major questions addressed in the present paper, which seeks orbital selection rules for ET and polar TS structures for reactions of anion radicals with alkyl halides.

In a recent VB analysis^{4a} of the ET–polar dichotomy it has been predicted that reactions between anion radicals and neutral molecules possess ET-TS's with an inherent propensity for an inner-sphere structure.^{4b} The present paper tests the prediction by computational means using the model ET and SUB reactions of the CH₂=O^{•-} anion radical and the CH₃Cl molecule. It is found that the ET-TS is a tightly bonded species with robust stereo- and regiochemistry, and these features are reflected in the isotope effects and entropy of activation of the ET reaction. What is more important, the paper presents the first computational evidence for the existence of orbital selection rules that govern the stereoselectivity and regioselectivity of the ET-TS and its isomeric SUB-TS.

Computations were performed with the Gaussian 92 series of programs.⁵ Geometries were gradient optimized and characterized by frequency analysis, initially at UHF/6-31G* and then at UMP2(FC)/6-31+G*. Reaction pathways were ascertained by IRC path following, which is a standard computational procedure for assigning a TS to a particular mechanism.⁶ The two theoretical levels, UHF/6-31G* and UMP2(FC)/6-31+G*, led to an identical mechanistic dichotomy including the regio- and stereoselectivity of the respective TS structures. The spin contamination of the critical species for the ET and polar

mechanisms is small ($\langle S^2 \rangle \approx 0.760-0.768$). Single-point calculations at the QCISD(T)(FC)/6-31+G* level were performed on the UMP2(FC)/6-31+G* optimized structures. The relative energies of the critical species obtained at the UMP2(FC)//UMP2(FC)/6-31+G* level were maintained at the higher levels up to QCISD(T)(FC)/6-31+G*//UMP2(FC)/6-31+G*. Isotope effects⁷ were computed with Eyring's equation, at the UMP2/6-31+G* level using scaled and unscaled frequencies.

The continuous solid line in Figure 1 shows the computed energy profiles (ascertained by IRC) of the dissociative ET⁸ and the S_N2-type SUB mechanisms. Both mechanisms start from a common reactant cluster (C_R) and go on to product clusters of the ET and SUB varieties (C_{ET}, C_{SUB}) through two corresponding TS's. The product clusters can further separate out to the corresponding ET and SUB products (P_{ET}, P_{SUB}); the latter correspond to the O-alkylation product, in accord with experimental^{9,10} systems. *Despite numerous searches, no direct SUB pathway could be found for C-alkylation.*^{11a} The only way to obtain C-alkylation, P_{ET/SUB} (the preceding cluster is not shown in the figure), is via the C_{AT}-TS by CH₃ radical attack on CH₂O, within the cluster C_{ET}. The analogous O_{AT}-TS, corresponding to CH₃ attack on the O-end of the CH₂O molecule within the cluster C_{ET}, is much higher in energy than C_{AT}-TS.^{11b}

The key structures of the two mechanisms, the C_R cluster and the ET- and SUB-TS's, are drawn in Figure 1. The ET-TS has a backside stereochemistry, and its tight bonding is apparent by comparing it to C_R. Thus, the anion radical moiety undergoes a major reorganization from an O- -C-Cl orientation in C_R to a C- -C-Cl orientation in the ET-TS. This reorganization is attended by a reduction of the C-C distance from 3.456 Å in the C_R cluster to 2.521 Å in the ET-TS, thereby indicating a major driving force to achieve bonding in the ET-TS. Indeed, as is shown in Table 1, the ET process is characterized by a negative entropy of activation that is comparable to the corresponding value for the SUB process.¹² Similarly, the central carbon isotope effect (α -(C¹²/C¹³)) value for the ET process is virtually identical to the value for the SUB process and is in the range accepted for polar TS's in experimental S_N2 systems.¹³ Attempts to find ET saddle points by approach through the O-end of the anion radical or in nonlinear trajectories failed. The only ET-TS that could be located is the one drawn in Figure 1. It follows therefore that the ET-TS does not conform with the traditional outer-sphere description, but is well bonded with a definitive structure and a robust stereochemistry.

The striking features in Figure 1 are the contrasting regiochemistry and orientation of the two TS's. While the ET-TS involves C- -C- -Cl bonding obtained via C-attack and π -ori-

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(11) (a) An exhaustive search was carried out to locate the direct C-alkylation TS from C_R in many different orientations. All attempts resulted in high-energy structures which collapsed either to the ET-TS or to C_{AT}-TS, which, in turn, is connected to the ET cluster. There is no direct C-alkylation pathway, and this is an indication of the importance of the selection rules. (b) For these two TS's the UMP2(FC) (S^2) values are 0.88 (C_{AT}-TS) and 0.965 (O_{AT}-TS). Spin-projected energies PMP2 and PMP3 are necessary to obtain consistency with the QCISD(T) relative energies. For the (C_{AT}-TS) structure: Gonzalez, C.; Sosa, C.; Schlegel, H. B. *J. Phys. Chem.* **1989**, *93*, 2435.

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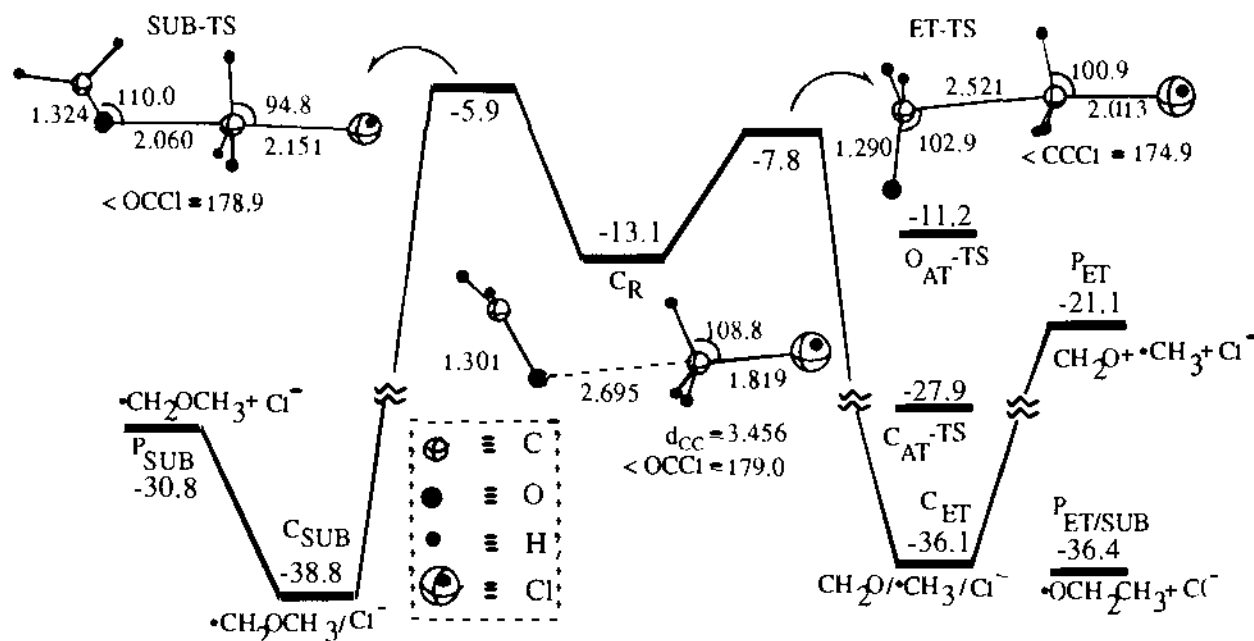


Figure 1. QCISD(T)(FC)/6-31+G**/UMP2(FC)/6-31+G* energy profile for the ET and SUB mechanisms. Energies (in kcal/mol) are relative to the reactants. Only the three key structures are shown.

Table 1. Entropies of Activation and Isotope Effects for the SUB and ET Processes^a

reactn	ΔS^\ddagger , eu ^{b,c}	$\alpha\text{-(C}^{12}\text{/C}^{13})^r$	$\alpha\text{-(CH}_3\text{/CD}_3)^r$
SUB	-26.3 (-26.7)	1.133 (1.054)	0.913 (0.923)
ET	-24.2 (-24.6)	1.119 (1.051)	1.122 (1.113)

^a The parameters correspond to the process $R \rightarrow P$. ^b The standard state is 1 M at 298.15 K. ^c Results in parentheses are obtained with frequencies scaled by the factor 0.8929.

entation of the formaldehyde moiety, the SUB-TS involves O-C-Cl bonding, achieved by O-attack and a virtually in-plane orientation of the formaldehyde moiety. Table 1 further shows that these structural features of the two TS's can be probed by $\alpha\text{-(CH}_3\text{/CD}_3)$ isotope effects that are inverse for the SUB mechanism and normal for the ET mechanism. These $\alpha\text{-(CH}_3\text{/CD}_3)$ isotope effect patterns correlate with the higher positive charge density on the CH₃ group and with the shorter C-H bond lengths in the SUB-TS.¹⁴

These contrasting structural features of the two TS's follow a recent prediction based on the VB configuration mixing (VBCM) analysis of the ET-SUB dichotomy in analogous reactions between anion radicals ($A^{\cdot-}$) and alkyl halides (RX).^{4a,15} The VB model allows one to resolve the complex orbital interactions and to single out reaction-specific orbital selection rules that dominate the structures of the ET-TS and the SUB-TS. This is done by analyzing the respective resonance interactions of the ET and SUB VB configurations, each in turn with the reactant VB configuration.¹⁵ In the present case, the reactant configuration is described by the electronic occupation, $n_0^2\pi^*_{\text{CO}}\sigma_{\text{CCl}}^2$, where n_0 and π^*_{CO} are the respective lone pair and π -antibonding orbitals of the formaldehyde moiety, while σ_{CCl} and σ^*_{CCl} are the corresponding orbitals of the C-Cl moiety of CH₃Cl. Similarly, the ET configuration is given by $n_0^2\sigma_{\text{CCl}}\sigma^*_{\text{CCl}}$, while the SUB configuration is given by $\pi^*_{\text{CO}}n_0\sigma_{\text{CCl}}\sigma^*_{\text{CCl}}$. Following the VB mixing rules^{4a} it is predicted that the structure of the ET-TS will be determined by optimizing the $\pi^*_{\text{CO}}(\text{CH}_2=\text{O}^{\cdot-})-\sigma^*_{\text{CCl}}(\text{CH}_3\text{Cl})$ overlap, but that of the SUB-TS will be determined by optimizing the $n_0(\text{CH}_2=\text{O}^{\cdot-})-\sigma^*_{\text{CCl}}(\text{CH}_3\text{Cl})$ overlap.

These reaction-specific resonance interactions for $\text{CH}_2=\text{O}^{\cdot-}$ and CH_3Cl are depicted in Figure 2. It is seen that the resonance interaction for the ET-TS, being proportional to the overlap of π^*_{CO} with σ^*_{CCl} , will lead to the ET-TS that possesses a backside stereochemistry with C-C-Cl bonding involving a π -plane attack of the formaldehyde moiety. On the other hand, the structure of the SUB-TS will be determined by the overlap

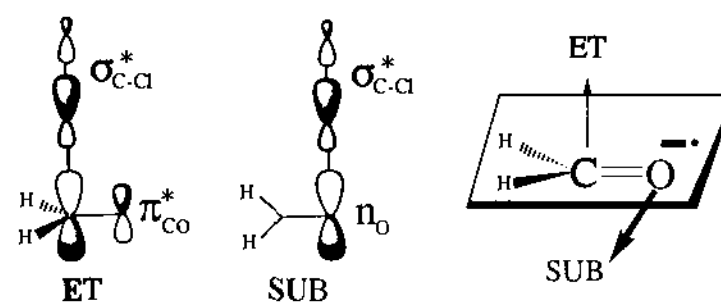


Figure 2. The resonance interactions^{4a,15} for the ET-TS and SUB-TS. The predicted regioselectivities and trajectories of attack are shown on the right.

of the lone pair orbital, n_0 with σ^*_{CCl} , and will therefore require a backside stereochemistry involving O-C-Cl bonding and an in-plane attack of the formaldehyde moiety. Consequently, the SUB pathway that is dominated by the $n_0-\sigma^*_{\text{CCl}}$ interaction behaves effectively like a normal S_N2 process possessing a 4-electron/3-center TS. On the other hand, the ET pathway that is controlled by the $\pi^*_{\text{CO}}-\sigma^*_{\text{CCl}}$ interaction involves a 3-electron/3-center TS. It is apparent that the predictions of the VBCM model coincide beautifully with the computational results, and the stereochemistries of the ET and SUB pathways follow orbital selection rules which are dictated by the resonance interactions of the respective TS's.

In summary, our study indicates that, at least in the model system of the $\text{CH}_2=\text{O}^{\cdot-}$ anion radical and the CH_3Cl molecule, the orientation, regioselectivity and stereoselectivity of both ET and SUB reactions are determined by reaction-specific orbital selection rules. These selection rules seem powerful enough to preclude other structural variants for the ET- and SUB-TS's. We are presently exploring structural consequences¹⁰ of the orbital selection rules which might further establish the ET-SUB dichotomy on orbital symmetry principles.¹⁶ It is time, we feel, to reorient some of the ET studies in ion radical chemistry toward the structural domain.

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Supplementary Material Available: UHF/6-31G* and UQCISD(T)/6-31+G**/UMP2/6-31+G* results (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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