Reaction Selectivity

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Chemical Selectivity through Control of Excited-State Dynamics**

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conformation selectivity · conical intersections · orbital alignment · reaction mechanisms · stereodynamics

The chemo-, regio-, and stereoselectivity of chemical reactions has always been at the core of chemical research. The traditional design of selective reactions is based on thermal chemistry where the vibrational energy distribution of the reactant in its electronic ground state is governed by Boltzmann statistics. Under these conditions, the transition state theory (TST) proposed by Eyring, Evans, and Polanyi[1] is obeyed, and the reaction rate is determined by the probability to overcome the energy barrier dividing the reactant and product wells on the potential energy surface (PES).[1] Under kinetic control, selectivity is achieved by the use of catalysts, the introduction of activating and protecting functional groups, and the variation of the solvent to modulate the difference in the barriers of the possible competitive reactions.[2] In spite of these established concepts, it has been shown that thermal reactions taking place on a flat PES, for example when diradicals or radical pairs are formed, do not obey TST. To explain the observed selectivity, Carpenter et al. proposed the novel concept of dynamic effects arising from a nonstatistical thermal energy distribution on the internal (vibrational) degrees of freedom of the reactive intermediates.[3]

Laser excitation of specific vibrational modes provides an alternative way to achieve selectivity through preparation of a nonstatistical vibrational energy distribution of the reactants, giving rise to what is called mode-selective chemistry.[4] In molecular beam experiments, it has been shown, for example, that the product outcome of the bimolecular collision $NH_3^+ + ND_3$ can be modified by selective excitation of either the NH_3^+ umbrella-inversion mode or its symmetric stretch mode.[5] Vibrationally mediated bond-selective dissociation has been also recently proved in heterogeneous catalysis, exciting specific vibrations of CHD_3 molecular beams impinging on a Ni surface.[6]

Also electronic excitation can be exploited to enhance chemical selectivity. In photochemistry, light absorption promotes the reactant to an excited electronic state that is associated with a different PES. On such a PES the original reactant structure does not correspond to an energy minimum giving rise to an acceleration downhill along specific molecular modes that become vibrationally excited and ultimately "reactive".[7] In fact, a nonstatistical energy distribution is easily obtained by ultrafast laser excitations[8] leading, in principle, to a new route to chemical selectivity. In the limit of an instantaneous laser pulse, the reactant is vertically excited into the excited electronic state [Franck–Condon (FC) principle] creating a population far from thermal equilibrium where few (FC-active) vibrational modes are "hot" while others are "cold". Recasting this qualitative picture in the theoretical framework of quantum dynamics, ultrafast (femtosecond timescale) laser pulses do not prepare a single eigenstate $|n\rangle$ but a nuclear wavepacket (WP), that is, a nonstationary superposition $|\psi(t)\rangle$ of states $|\psi(t)\rangle = \Sigma_n c_n(t)|n\rangle \exp[-iE_n t/\hbar]$ with coefficients $c_n(t)$ linked by well-defined phase relations (coherences).[9,10] The time-evolution of the WP has an approximate classical representation in terms of a set of trajectories released on the excited state PES whose initial positions and velocities "sample" the probability density of the quantum state, a distribution well localized in the phase space (see Figure 1).[11]

This localization allows us to describe the initial dynamics of the whole population (the WP) as the single (average) trajectory of a classical object on the excited PES. During its motion the WP can undergo chemical reactions that are not governed by TST (which concerns thermally equilibrated populations) but by the forces acting on the nuclei and by their velocities.[8] This dynamic regime persists until statistical equilibrium is restored through processes like decoherence (decay of the coherences) and intramolecular vibrational redistribution (transfer of populations); eventually the system

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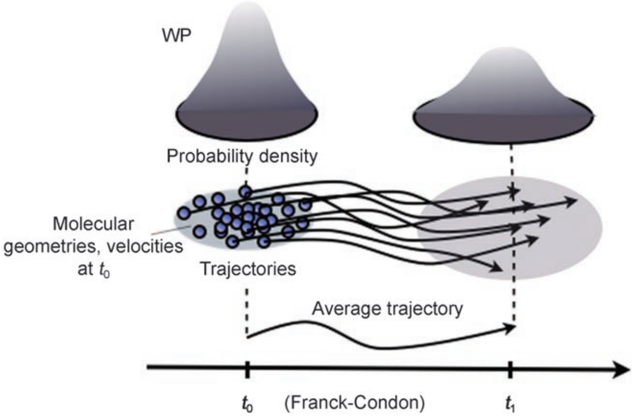

Figure 1. A representation of the time evolution of the wavepacket probability density and its representation in terms of classical trajectories sampling the initial density both in the coordinates and in the momenta space.

collapses into a Boltzmann energy distribution.[9] These thermalization processes that operate in a timescale from dozens of femtoseconds to dozens of picoseconds set a "lifetime window" for the occurrence of a chemical reaction in a nonstatistical regime. Femtochemistry is a recently born branch of chemistry that focuses on such ultrafast processes.[8]

Ultrafast photochemical reactions are made possible through nonradiative transitions that, ultimately, convert the photon energy into a nonstatistical distribution of vibrational energy of the electronic ground state. In the region of conical intersections, where the excited and ground states become degenerate,[12] these transitions are fully efficient. In nature, biological evolution has fostered high selectivity by "designing" ultrafast photochemical reactions mediated by conical intersection funnels. A well-known example is the stereoselective isomerization of the 11-*cis* double bond of retinal, the chromophore of the visual pigment rhodopsin.[13] Here the initial energy distribution on the FC-active modes undergoes a nonstatistical conversion prompting the reaction. According to a recent dynamic simulation carried out in our laboratories,[14] the excited PES induces, on a 150 fs timescale, a specific crankshaft motion which allows an effective and space-saving isomerization in the protein cavity.

Similar to thermal reactions, it is in principle possible to control the outcome of ultrafast photoreactions. An original approach recently presented relies on the effects of different conformations on the excited-state dynamics,[15,18] a possibility previously understated. The key idea is that, upon excitation, different conformers are promoted to different regions of the excited PES and may thus undergo different reactions. In 2002 Park et al.[15] reported conformation-selective pathways in the photodissociation of 1-iodopropane ions, where the *gauche* ions form 2-propyl ions while the *anti* ions form protonated cyclopropane ions. This finding was remarkable since conformers are characterized by small interconversion barriers, which in the ground state are overcome on a timescale much shorter than usually required for a thermal reaction. In contrast, in the excited state the ultrafast dynamics driven by the energy gradient on the PES may be faster than the conformer interconversion. This idea was proposed many years ago by Jacobs and Havinga, who cast the photochemical principle of the nonequilibration of the excited-state rotamers (NEER).[16] This principle explains a large body of data on polyene (e.g. hexatriene) product distributions.[17]

The photodissociation discussed in Ref.[15] takes place entirely in the electronic excited state. An alternative possibility has been recently discussed by Kim et al.,[18] who report conformer selectivity in the photodissociation of *gauche* and *cis* conformers of propanal cations, despite the fact that the actual reaction takes place on the ground PES, where the system has an excess energy of ≈ 3 eV and the minima corresponding to the two conformers are almost degenerate (within 0.03 eV).[18] Computer simulations have shown that the two conformers are excited in different regions of the excited PES where the energy gradients drive them to different conical intersections. The subsequent nonradiative transition to the electronic ground state deposits each conformer into a different dissociation channel on the ground-state PES, where conformer interconversion is no longer competitive.

In their interesting paper Lim et al.[19] present a different example of the control of excited-state dynamics. The key idea is somewhat analogous to conformation selectivity and relies on the structural effects of substitution. They consider the homolytic photodissociation of [S-D_1]thiophenol in a supersonic jet and control the alignment, with respect to the ring plane, of the singly occupied orbital (SOMO) of the phenylthiyl radical product.[20,21] An (n_π,σ^*) transition excites [S-D_1]thiophenol to the S_2 state, triggering a 100 fs dissociation of the D atom and the production of C_6H_5S radicals with the SOMO (mainly localized on the sulfur atom),[20,21] oriented either parallel ($\tilde{A}$ state) or perpendicular ($\tilde{X}$ state) to the molecular plane. In analogy to what was shown for phenol,[22] most of the chemistry of this process is described by the two-mode model sketched in Figure 2. Upon S–D bond elongation, the $\tilde{X}$ and $\tilde{A}$ PES form a conical intersection (CI)[19,22] at planar configurations (C-C-S-D 0°) that induces electronic transitions, thus explaining the production of two different C_6H_5S species, $\tilde{X}$ and $\tilde{A}$, which diabatically correlate with the FC second excited (S_2) and ground (S_0) states, respectively.

In their strategy for reaction control, Lim et al. rely on the fact that the probability of the electronic transition increases when the WP passes closer to the CI, and they modify its motion by changing its initial position (i.e. the S_0 equilibrium structure) through substitution. In the parent C_6H_5SD, planar arrangements in which the SD moiety is coplanar with the phenyl ring are energetically favored in both the S_0 and S_2 states. Therefore, the initially prepared WP moves away from its original equilibrium position along the SD coordinate only, remaining substantially planar. The subsequent decay at CI (Figure 2 A) leads to an almost equal product yield for the two species (57 % $\tilde{A}$ C_6H_5S and 43 % $\tilde{X}$ C_6H_5S).[19] The insertion of an electron-releasing group in the *para* position modifies the WP dynamics by shifting the in-plane S_0 equilibrium position of SD toward perpendicular arrangements, while leaving the preference for an S_2 planar configuration unaltered. Thus, for

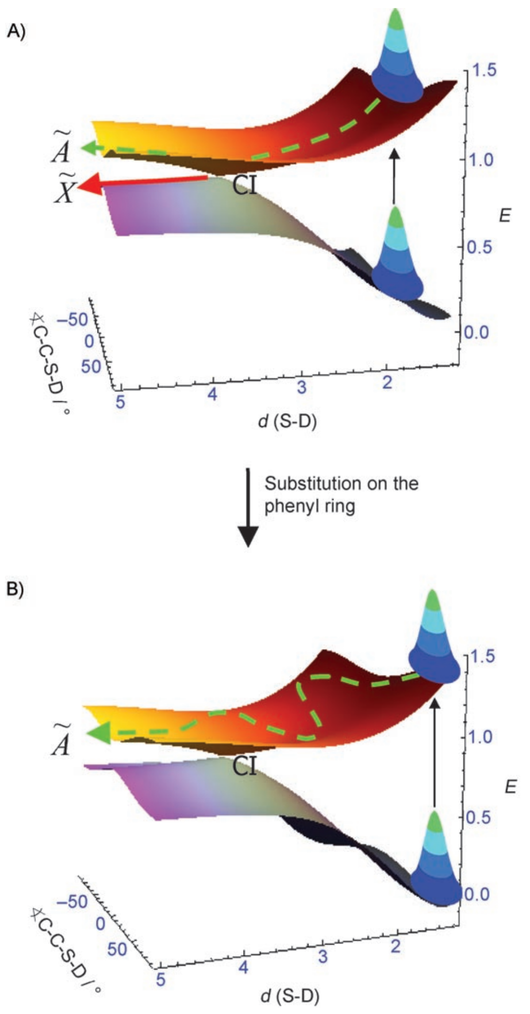

Figure 2. Two-dimensional model for the photodissociation of XC_6H_4SD. A) In the case of C_6H_5SD, planar configurations (C-C-S-D 0°) are energetically favored on both potential energy surfaces. The wavepacket (WP) passes through the conical intersection (CI), splits, and gives rise to two product species ($\tilde{X}$ and $\tilde{A}$), one on each PES. B) In a borderline situation similar to that of $CH_3OC_6H_4SD$ the minimum-energy structures along the C-C-S-D axis are at 90° and 0° in the ground and excited states, respectively. The WP oscillates along C-C-S-D and may miss the conical intersection remaining on the excited PES, thus giving rise to the $\tilde{A}$ product species only.

the case of the methoxy derivative, $CH_3OC_6H_4SD$, where the S_0 equilibrium position has an C-C-S-D angle of 73°, the WP average motion also involves the C-C-S-D angle, yielding a very different product ratio (91% $\tilde{A}$ $CH_3OC_6H_4S$) which documents a major tendency to remain in the $\tilde{A}$ state.[18]

Lim et al.[19] explain the behavior of $CH_3OC_6H_4SD$ by noticing that the oscillations along C-C-S-D torsion induces a broadening of the WP (i.e. in classical terms the trajectories that represent WP spread in the space), so that only a limited amount of the population enters the CI region and decay. In principle, beyond the spreading (whose extent depends on the shape of the excited-state PES), a direct effect of oscillations could come into play. In fact, also a well-localized WP might miss the CI, partially or totally, depending on the ratio between the time required to elongate the S−D bond to the CI value and the torsional period (see Figure 2B). A detailed quantum-dynamics simulation of the process studied by Lim et al.[19] could clarify the role of the oscillations and spreading of the WP in determining the product outcome. In conclusion, the classical substituent effects described in organic chemistry textbooks[2] seem to also control the selectivity of nonstatistical reactions.

A further point of interest in the selectivity effect reported by Lim et al.[19] comes from the object of the control, that is, the preparation of radicals that differ for the orientation of an atomic-like SOMO. Studies on reaction stereodynamics,[23] that is, on the effects of the approach geometry of the reagents in molecular beams, have shown that preorientation of the reactants can modify the product outcome.[4] This phenomenon has been observed not only by orienting the colliding molecules, but also by aligning the SOMO of open-shell systems with respect to a laboratory frame, as in the reaction $Ca(^1P) + CH_3I$.[24] Lim et al.[19] show that is possible to produce C_6H_5S radicals with a specific alignment of the SOMO with respect to the molecular frame, and they suggest that the two possible product species could have different stereodynamic reactivities in bimolecular collisions, metal-complexation reactions, and surface adsorption.[19–21]

While we agree with the authors, it seems apparent that such exciting possibilities require further studies. In fact, it will be necessary to investigate the stability of the $\tilde{X}$ and $\tilde{A}$ C_6H_5S species with respect to mutual interconversion driven by vibronic or rotoelectronic couplings. Indeed a sufficiently slow interconversion is a necessary prerequisite to allow the individual species to react independently and for the exploration of the stereodynamic consequences of the intramolecular alignment of the SOMO. Moreover, in the aim to obtain product selectivity, one should cope with the easy interconversion of possible products differentiated only by the orientation around the C−S single bond, if the rotation is not prevented by steric constraints.

An active research field generally referred to as quantum coherent control (CC)[24] follows a different route to laser-mediated chemical selectivity. It focuses on the optimization of the radiation source (a “physical” route)[25,26] more than on the optimization of the reactant itself (a “chemical” route) pursued by Lim et al.[19] To understand the basic idea we must recollect that a WP is a coherent superposition of states and is fully quantum mechanical in nature. Tailored laser pulses can establish suitable relationships among the coefficients of this superposition of states, creating constructive and destructive interferences that are able to guide the dynamics of the system.[25,26] Beyond that, if the laser pulse is intense, the time-dependent energy term introduced in the Hamiltonian of the reactant can remarkably modify in time the relevant PES, shaping energy barriers and reactive channels, and driving, ultimately, the molecule toward the required target.[27] The previously discussed routes to chemical selectivity all focus on the preparation of suitable states of the system that then react spontaneously. At variance, an additional characteristic of CC is that tailored laser pulses may in principle assist the reaction during its whole time evolution.[4] In 1998 Assion et al.[28] first used pulse shapers[29] to achieve the CC of a chemical reaction, namely the competitive dissociation of metal complexes. Following an original idea of Jusdon et al.,[30] they implemented self-learning algorithms to adjust the laser pulse in an iterative manner, on the ground of feedback signals from the reacting system itself.[29] Like the "chemical routes" discussed above, a major problem of the selectivity enhancement by means of CC is decoherence, which destroys the interferential features in the WP. The more complex the environment, the more effective decoherence, thus setting a lifetime window to its applicability. Nonetheless, theoretical investigations have suggested that appreciable control can still be obtained in the presence of partial decoherence;[31] and this was actually witnessed in recent experiments on sizeable molecules in solution[32] and in a protein environment.[33] We believe that in the near future a synergistic application of the "chemical" and "physical" routes, exploiting the possibilities of both chemical modifications and optimal generation of laser pulses, will lead to improved results in the field of photochemical selectivity.

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