Simple Fitting of Energy-Resolved Reactive Cross Sections in Threshold Collision-Induced Dissociation (T-CID) Experiments

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An operationally much simpler method for the extraction of thermochemical data from energy-resolved collision-induced dissociation cross sections, which is specifically designed for ligand binding energy determinations by tandem mass spectrometry, is presented. Compared to previous methods available in the literature, the present method has three advantages: (i) A more realistic treatment of the electrostatic potential for the approach of the ion to the collision partner leads to a better, nonempirical threshold function, allowing fitting of the cross section over the entire energy range rather than just the onset. (ii) Treatment of the kinetic shift with a new model for the density-of-states function eliminates the need for explicit entry of frequencies for the starting ion or the transition state without loss of accuracy relative to direct state counts. (iii) Data fitting using Monte Carlo simulation and a genetic algorithm instead of the usual Marquardt−Levenburg least-squares routines not only produces an equivalent fit but also produces statistically relevant error bounds on the derived fit parameters. Although the method is conceived for medium-to-large organometallic complexes, the theory is general enough to be appropriate for a wide range of binding phenomena of a small molecule to a larger one observed in mass spectrometry.

Introduction

Systematic determinations of ligand binding energies in medium-to-large-sized organometallic complexes have been rare, with methodological limitations playing a significant role in the paucity of quantitative data. Mass spectrometric methods, including gas-phase equilibra in flowing afterglows[1] and other mass spectrometers, bracketing with ion−molecule reactions,[2] and Cooks' kinetic method,[3] have all been applied at one point or another. Energy-resolved collision-induced dissociation cross-section measurements have been employed for a range of smaller complexes,[4] but the application to species directly involved in homogeneous catalysis has just begun.[5−9] The method measures the energetic threshold for collision-induced dissociation (CID) of an ion under well-defined conditions from which the threshold energy, E_0, can be extracted by a deconvolution procedure. In practice, the deconvolution is usually done with the program CRUNCH, developed by Armentrout and co-workers.[10] We report an operationally much simpler method for the extraction of thermochemical data from energy-resolved collision-induced dissociation cross sections, which is specifically designed for ligand binding energy determinations by tandem mass spectrometry. Compared to CRUNCH, the present method has three advantages: (i) A more realistic treatment of the electrostatic potential for the approach of the ion to the collision partner leads to a better, nonempirical threshold function, allowing fitting of the cross section over the entire energy range rather than just the onset. (ii) Treatment of the kinetic shift with a new model for the density-of-states function completely eliminates the need for explicit entry of frequencies for the starting ion or the transition state without loss of accuracy relative to direct state counts. (iii) Data fitting using Monte Carlo simulation and a genetic algorithm instead of the usual Marquardt−Levenburg least-squares routines not only produces an equivalent fit but also produces statistically relevant error bounds on the derived fit parameters. Although the method is conceived for medium-to-large organometallic complexes, the theory is general enough to be appropriate for a wide range of binding phenomena of a small molecule to a larger one observed in mass spectrometry. Validation of an implementation of the new model in the program L-CID (**l**igand **c**ollision-**i**nduced **d**issociation) with several large data sets for which CRUNCH fits have already been done indicates that numerically similar results with similar uncertainty bounds are achieved with a substantial reduction in time and effort. The advantage becomes larger as the size and complexity of the ion increase. The improved ease-of-use in L-CID should make energy-resolved CID cross-section measurements much more routine in catalysis research.

Theory and Program Architecture

Construction of an efficient code for the deconvolution of the energy-resolved CID cross sections requires physically realistic models for several of the component processes in the CID event. Within the overall architecture of L-CID, several novel theoretical or computational approaches are taken, which altogether produce the simple method claimed in the Introduction. The individual processes modeled in L-CID are shown graphically in Scheme 1, together with indicators showing where the model differs significantly from the comparable approach in CRUNCH. It should be noted here that CRUNCH, as the current state-of-the-art in deconvolution of energy-resolved CID cross sections, must necessarily be taken as the reference for comparison. As indicated in the Introduction, there are three broad areas in which L-CID differs from CRUNCH. The first is the treatment of the ion−molecule collision dynamics. The

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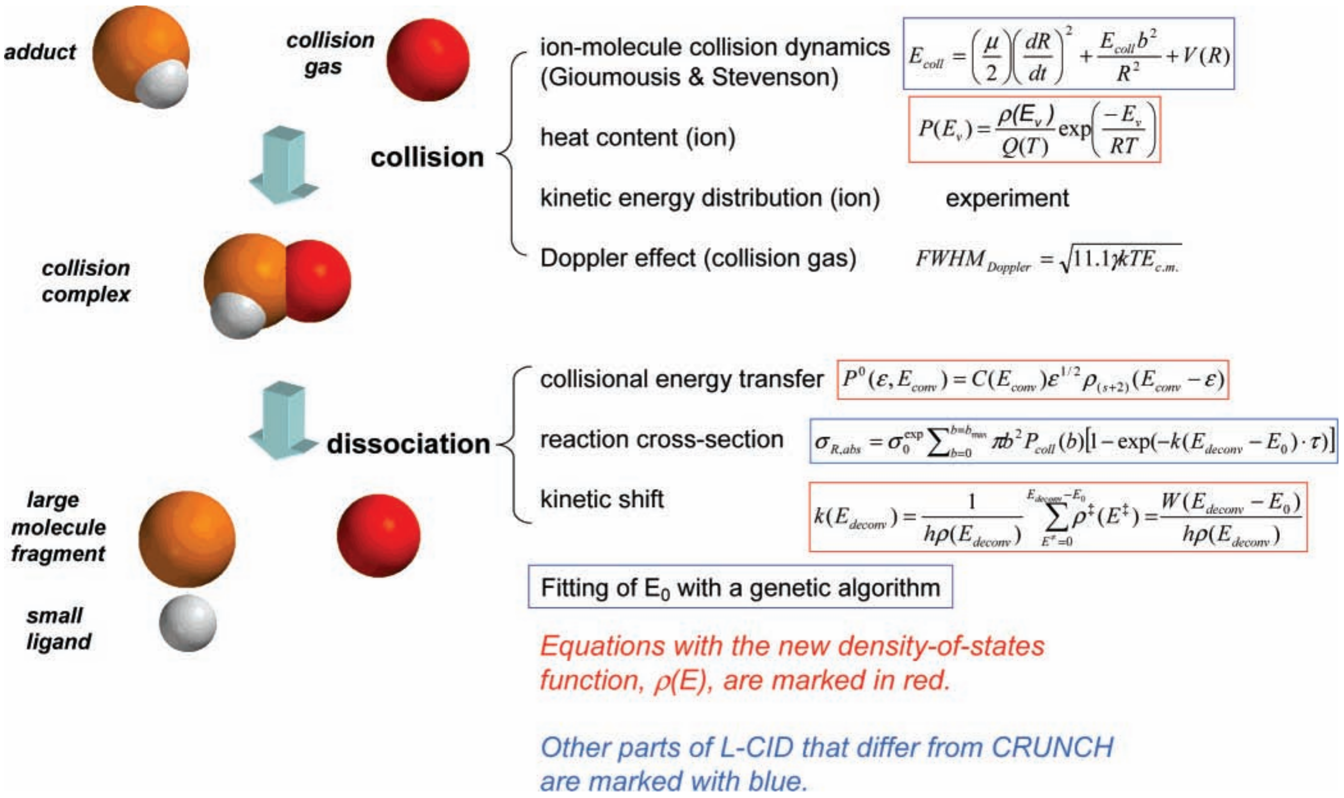
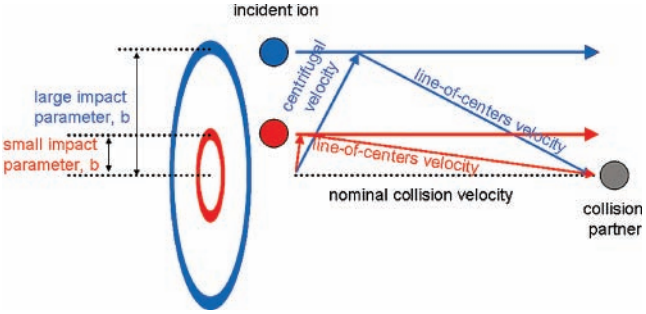
SCHEME 1: Component Processes in L-CID[a]



[a] Modules in which the new approximation for the density-of-states function, $r(E)$, is used are marked in red. Further modules where L-CID differs significantly from CRUNCH are indicated in blue.

SCHEME 2: Vector Diagram Showing the Partitioning of the Incident Velocity into a Component along the Line-of-Centers and a Centrifugal Component, as a Function of Impact Parameter[a]



[a] For a given nominal collision energy, a larger fraction of the translational energy is available for reaction when the impact parameter is small, but there are many more collisions with large impact parameter.

threshold function in CRUNCH was originally taken to be that for a line-of-centers collision model, modified with a fitted exponent to produce a sigmoidal function with variable steepness.[11] In later discussions, no specific physical interpretation is given for the exponent. In L-CID, the ion−molecule collision is treated with the electrostatic theory by Giomousis and Stevenson.[12] A complete development of the operational equations is given in the Supporting Information.

It is important to note that the model of Giomousis and Stevenson[12] properly treats the centrifugal barrier in the collision by partitioning the total collision energy between the fraction that is available for reaction and the remainder that is sequestered in overall rotation of the collision complex, as depicted in Scheme 2. For large impact parameters, which from geometric arguments comprise the majority of collision events, the fraction of the collision energy unavailable for reaction becomes predominant, producing a very large effect on the shape of the threshold function. Without this proper treatment, which derives from conservation of angular momentum, the cross sections rise much too steeply, making it impossible to fit the entire curve up to the plateau where the cross section flattens out. On the other hand, the inclusion of angular momentum effects in the collision dynamics produces a threshold function, which naturally shows the proper shape over the entire energy range with no empirical corrections and, importantly, no fit parameters.

The effect can be minimized if one fits only the part of the curve where it just begins to rise from the baseline. This limited fitting, which is often done in CRUNCH, selects collision events with small impact parameters for which the centrifugal effects are the least severe, but there is no reason, a priori, to neglect the information in the rising portion of the curve and the plateau.

The second area in which L-CID differs from CRUNCH is in the treatment of the density-of-state function, $\rho(E)$. The density-of-states appears in several parts of the deconvolution, most prominently in the quantitative estimation of the kinetic shift with statistical rate theory.[13] As had been first remarked by Chupka[14] and Rosenstock et al.,[15] a kinetic shift is the shift of an apparent threshold to higher energies that arises because the observed threshold is not the threshold at which dissociation begins, but rather the threshold at which dissociation becomes fast enough to be observed in the finite time window in the experiment. Especially for larger ions, the kinetic shift can reach the same order-of-magnitude as E_0, making reliable modeling of $\rho(E)$ of great importance for the overall code. In principle, $\rho(E)$ appears also in the computation of the internal energy

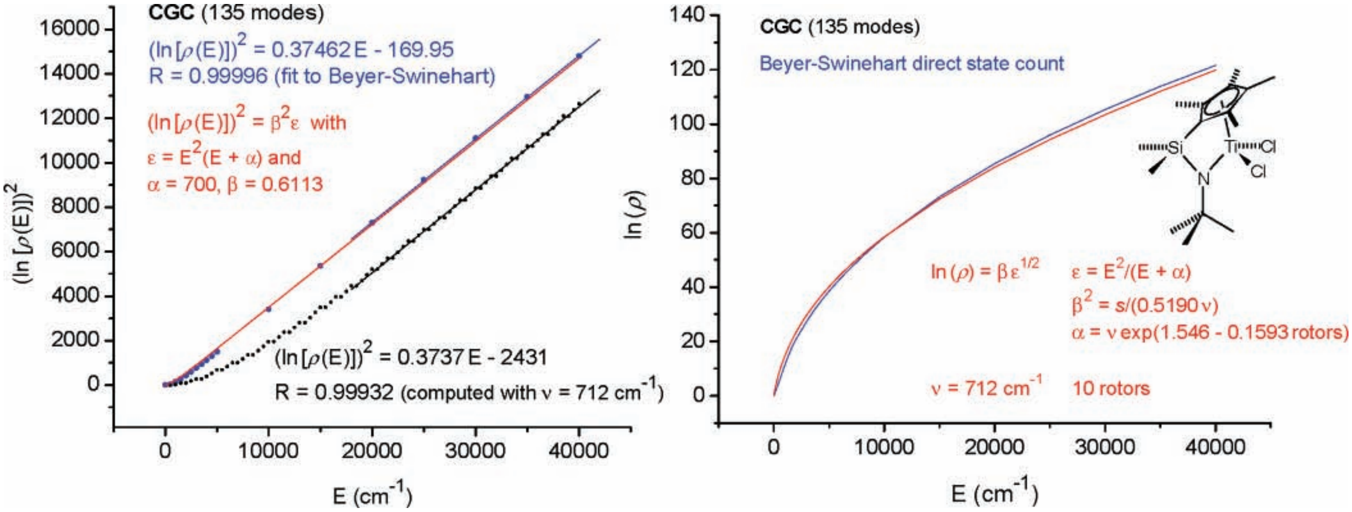


Figure 1. Dependence of the density-of-states function, $\rho(E)$, on the available energy for a constrained-geometry catalyst (CGC). Results computed using an explicit state count with the Beyer−Swinehart algorithm are indicated in blue. Results from an uncorrected single frequency fit are shown in black. Red indicates the computed density-of-states using the effective frequency approximation, corrected for the "graininess" at lower energies. The red line in the left-hand panel shows the result optimized to reproduce the blue CGC data. The red line in the right-hand panel shows the result using fitting parameters that are optimized against the entire reference set of molecules.

content of the incident ion—its heat capacity—as well as in the partitioning between internal energy in the ion and relative translation of the ion and departing collision partner energy in the inelastic collision. The latter consideration is a small, but not insignificant, effect, that is nevertheless treated properly in L-CID by means of a kinetic energy release distribution (KERD) in the framework of statistical rate theory, which also requires a good model for $\rho(E)$. CRUNCH takes the Beyer−Swinehart direct state count or the Whitten−Rabinovitch approximation for $\rho(E)$, both well-established and theoretically justified.[16] The disadvantage of both approaches is that explicit frequencies for the ion and the transition state are required, which, in turn, necessitate electronic structure calculations prior to deconvolution of experimental data. For larger, more complicated organometallic ions built around transition metal centers, the quantum chemical calculation, practically limited to the DFT level, can become a substantial undertaking itself. To simplify the operational use of a deconvolution scheme, one would want to subsume the structural information into a fit parameter that is directly derived from the experimental cross sections without prior recourse to structure calculations. The qualitative justification for this goal is that one assumes, when a molecule is large enough, sufficient averaging occurs so that the precise value of one particular frequency for a given normal mode does not matter much. One hopes that $\rho(E)$ can be derived from a single effective frequency, ν, that may be used as the fit parameter in the internal energy content of the ion, the inelastic collision's energy partitioning, and the kinetic shift. Other input information would necessarily be the number of degrees of freedom and, perhaps, some minimal structure-based index. An interesting indication that this might work came in a comment made by T. Baer,[17] who pointed out that canonical RRKM theory, for which the calculated rate depends on the density of states and the sum of states, which in turn depend on explicit frequencies, can be reduced to transition-state theory. Given that transition-state theory is fundamentally a two-parameter model, that is, $\Delta H^\ddagger$ and $\Delta S^\ddagger$, one would surmise that it should be possible to model microcanonical RRKM rates and, by extension, $\rho(E)$, with only two variable fitting parameters. One of the two parameters is the threshold energy, E_0, which we seek to extract from the experimental cross sections. The other could be the effective frequency, ν. The two suggested parameters are in fact closely related to the enthalpy and entropy of activation, respectively, which provides a physical basis for believing that the approximation could work. There is a single report of a two-frequency RRKM calculation,[18] which suggests that there is a high probability that the effective-frequency approximation will prove to be adequate for modeling $\rho(E)$. The latter was especially interesting because the modeling of unimolecular dissociation of highly excited polynuclear aromatics (PAHs) in competition with radiative deactivation is completely analogous to the calculation of reaction cross sections with a kinetic shift. The construction of a robust treatment of $\rho(E)$, as a function of an effective frequency, ν, is detailed in the Supporting Information, with all of the reference data, benchmarks, and test results. Figure 1 shows the data for one of the 22 reference molecules used to construct the approximation.

The final function approximating $\rho(E)$, with contants obtained from the set of 22 reference molecules, is given in eq 1

$$\rho(E) = \exp\left[\left(\frac{E^2 s}{0.5190\upsilon[E + \upsilon\exp(1.546 - 0.1593\ \text{rotors})]}\right)^{1/2}\right] \qquad (1)$$

in which the energy and frequency are expressed in cm^{-1}, s is the number of vibrational degrees of freedom ($3N - 6$ for N atoms), and the number of rotors is simply read from the structure. With an expression for the density-of-states function, $\rho(E)$, the computation of the internal energy content of the ion simply follows from a Boltzmann distribution based on the temperature of the manifold in which the ion is formed and thermalized prior to extraction and collision

$$P(E_\upsilon) = \frac{\rho(E_\upsilon)}{Q(T)}\exp\left(\frac{-E_\upsilon}{RT}\right) \qquad (2)$$

where the $Q(T)$ is the vibrational partition function at absolute temperature, T, and R is the gas constant. The kinetic energy release distribution (KERD) in the inelastic collision (of the incident ion with argon or xenon) is modeled using the expression derived from statistical rate theory[19]

$$P^0(\varepsilon, E_{\text{conv}}) = C(E_{\text{conv}})\varepsilon^{1/2}\rho_{(s+2)}(E_{\text{conv}} - \varepsilon) \qquad (3)$$

and then subtracted from the total available energy for reaction, energy going into relative translation of the rare gas atom and the energized ion being, of course, unavailable for subsequent reaction of the ion. Finally, the kinetic shift in the dissociation event is incorporated into the reactive cross section, $\sigma(E)$, via the microcanonical RRKM rate for dissociation,[16] $k(E)$, within the instrument-dependent time window, τ, which is integrated over the distribution of impact parameters, b

$$\sigma_{R,abs} = \sigma_0^{\exp} \sum_{\mathrm{b}=0}^{b=\mathrm{b}_{\max}} \pi b^2 P_{\mathrm{coll}}(b)[1 - \exp(-k(E_{\mathrm{deconv}} - E_0) \cdot \tau)] \tag{4}$$

where

$$k(E_{deconv}) = \frac{1}{h\rho(E_{deconv})} \sum_{E^{\ddagger}=0}^{E_{deconv}-E_0} \rho^{\ddagger}(E^{\ddagger}) = \frac{W(E_{deconv} - E_0)}{h\rho(E_{deconv})} \tag{5}$$

in which h is Planck's constant and W is the sum of states at the transition state. The microcanonical RRKM rate is computed with the assumption that the ratio of rotational partition functions is close to unity, which is justified for the case of a small ligand dissociating from a larger organometallic complex, the moments of inertia of the transition state not deviating much from those of the ion due to the disparity in sizes between the ligand and the complex. Other factors contributing to the energy available for dissociation, for example, the thermal motion of the collision gas and the kinetic energy distribution of the incident ions, are handled conventionally as they were in CRUNCH.

The third major area distinguishing L-CID from CRUNCH appears in the consolidation of all the various factors with optimization of the fitting parameters. Because variation of the effective frequency, ν, and the threshold energy, E_0, affects the density of states that appears, not only in the kinetic shift but also in the internal energy content and the kinetic energy release distribution earlier in the program, the fitting must be done to self-consistency. The conventional Marquardt−Levenburg nonlinear least-squares routine[20] would be poorly suited for the task given that the optimization would require the partial derivatives of the error function with respect to the fitting parameters. Because of the multiple places where ν enters into L-CID, analytical derivatives would be unrealistic. Numerical differentiation can be done but often leads to computational instability. Accordingly, a least-squares optimization of the parameters is done by way of a Monte Carlo simulation and a genetic algorithm.[21] Each of the various distributions, for example, ion kinetic energy, ion internal energy, Doppler broadening, kinetic energy release, and impact parameter, is convoluted together numerically to produce a distribution that is then used to create, for a given nominal collision energy, an ensemble of 10000 simulated collision events, each with a slightly different energy available for reaction. For a single nominal collision energy, eq 4, applied to the ensemble of simulated collision events, yields a distribution of reactive cross sections, the mean and variance of which are then used in the subsequent optimization procedure. The nominal energy is then stepped by a small increment, and another ensemble of simulated collision events is created. In total, for a typical experiment, several million simulated collision events are modeled in each iteration. The "trial" energy-resolved CID cross section is then constructed from the Monte Carlo simulations for each nominal energy and compared to the experimental curve in the given iteration. The genetic algorithm optimizes the two parameters, ν and E_0, by a biologically inspired, diversity-based process of mutation, crossover, "mating," under selection pressure so that the statistical variance of the simulated cross section against the experimental curve is minimized.[21] The procedure iterates over generations until the variance falls below the experimental variance of the data points themselves or the iteration is terminated manually. Because of the diversity-based optimization, values of ν and E_0 each have their own distributions, from which statistically valid uncertainty bounds may be derived. The genetic algorithm is described in more detail in the Supporting Information.

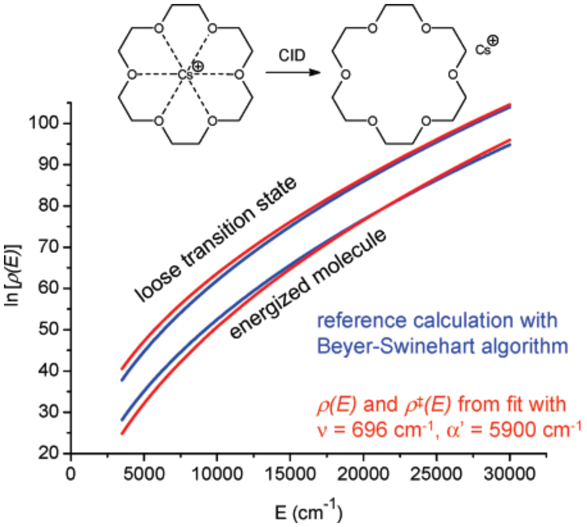


Figure 2. Plots of ln[$\rho(E)$] against E for [(18-crown-6)Cs]$^+$ and the transition state for dissociation. The benchmark densities-of-states, plotted in blue, were computed using the Beyer−Swinehart direct state count. The red plots correspond to the fit function in eq 1 with the single effective frequency of $\nu = 696$ cm^{-1}. The transition state model produced an α' parameter of 5900 cm^{-1}.

A final point on the construction of L-CID should be made. The density-of-states function for the transition state, $\rho^{\ddagger}(E)$, is constructed similarly to that for the ion itself, and furthermore, uses the same effective frequency, ν, under the assumption that most of the frequencies in a molecular species would not change much going from the starting ion to the transition state if the ion were large enough. Nevertheless, the function $\rho^{\ddagger}(E)$ shows a sensitivity to the "looseness" of the transition state, which cannot be subsumed into the fitting parameters, E_0 and ν, despite multiple attempts. Accordingly, we find that one additional structure-related parameter needs to be introduced. The parameter, α', with dimensions of energy (units of cm^{-1} in L-CID), is restricted to values 0−500 cm^{-1} for dissociations proceeding via a tight transition state; for loose transition states, α' is confined to the range of 5000−6500 cm^{-1} (see p S1-17 in the Supporting Information). The choice is set by a switch in L-CID after which this additional parameter is optimized under the above-mentioned constraint.

The FORTRAN source code for L-CID, as well as a compiled executable, are available upon request at the address listed for the corresponding author.

Results

From the physical point of view, the most severe approximation introduced in L-CID is the single effective frequency. Validation of eq 1 for cases outside the original set of reference molecules is done for two classes of ions: (i) ions that were published by Armentrout and co-workers as part of the demonstration for CRUNCH, for example, [(15-crown-5)Cs]$^+$

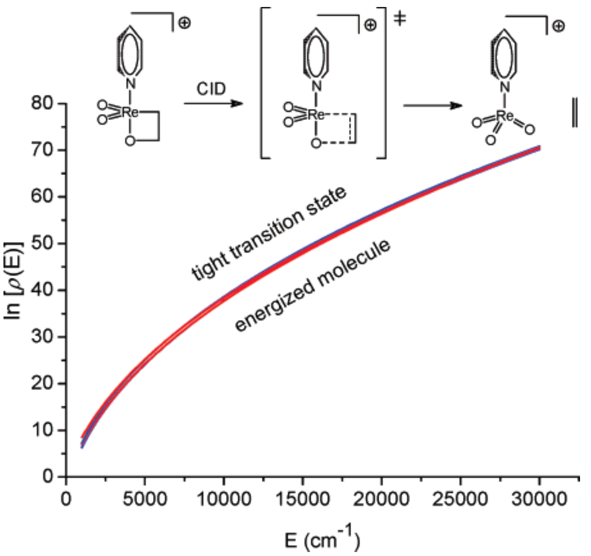


Figure 3. Plots of ln[$\rho(E)$] against E for [(pyr)Re($-$O$-$CH$_2$CH$_2$$-O-$)]$^+$ and the transition state for dissociation. The benchmark densities-of-states, plotted in blue, were computed using the Beyer$-$Swinehart direct state count. The red plots correspond to the fit function in eq 1 with the single effective frequency of ν = 790 cm^{-1}. The transition state model produced an α' parameter of 500 cm^{-1}. Because the transition state is tight, the density-of-states function for the energized molecule and that for the transition state are almost co-incident.

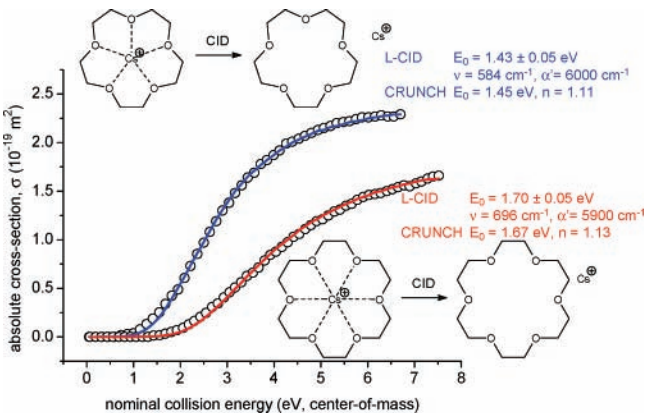


Figure 4. Energy-resolved CID cross sections for the dissociation of two different crown ether adducts of Cs$^+$. The curves were fit using either L-CID or CRUNCH, assuming a loose transition state for both complexes.

and [(18-crown-6)Cs]$^+$,[22] and (ii) medium to large metal$-$ligand complexes for which we have used CRUNCH to extract E_0 values relevant to organometallic reactions of Schiff base complexes of Pt(II)[9] and high-valent rhenium oxo complexes.[6] Because the approximations in the density-of-states calculations are the ones most in need of validation, representative comparisons of the ln[$\rho(E)$] versus E plots are shown for one example from each class in Figures 2 and 3. As can be seen from the two figures, the model gives good agreement for both the case of the loose transition state involved in the loss of Cs$^+$ from [(18-crown-6)Cs$^+$] and a tight one in which an intramolecular rearrangement prior to dissociation is rate-limiting.[23] Neither the crown ethers nor the rhenium oxo complexes are structurally related to any of the molecules in the reference set from which the fixed constants in eq 1 were determined, so one can consider the comparisons to be an unbiased control.

Having shown that the density-of-states function, $\rho(E)$, is well-modeled by the effective frequency approximation, the overall deconvolution of experimental cross sections was tested

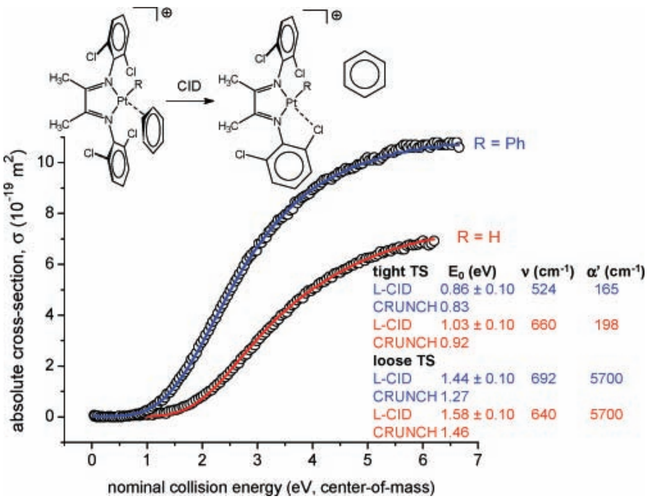


Figure 5. Energy-resolved CID cross sections for the dissociation of two different Pt(II) complexes with benzene. The curves were fit using either L-CID or CRUNCH, for both tight and loose transition states. Although the reaction is formally a dissociation, the rate-limiting transition state had been determined to be tight. The choice of transition state model cannot be determined unambiguously from the data themselves.

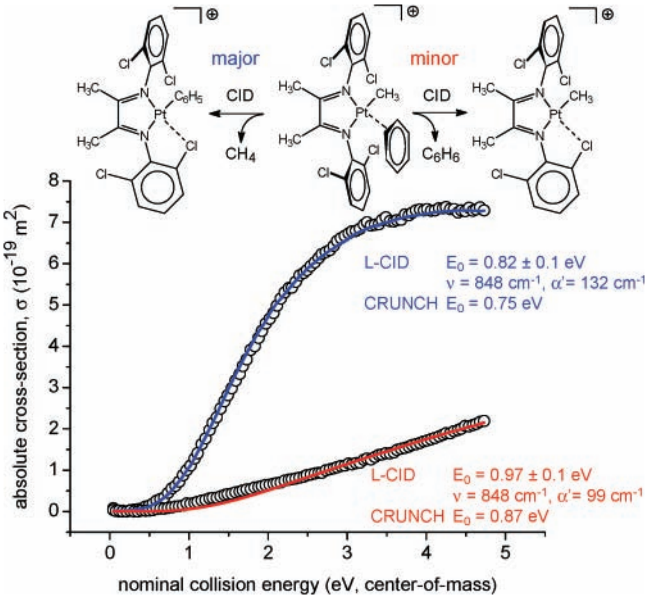


Figure 6. Energy-resolved CID cross sections for the competing dissociation of a single complex into two different products. The curves were fit using either L-CID or CRUNCH, for tight transition states as had been previously established. The two-channel procedure produces a fit which is statistically indistinguishable from the CRUNCH fit in that the variance between the fit and the data is less than the variance of the data themselves.

for crown ether adducts with cesium ions[22] as well as a series of Pt(II) complexes recently published by this group.[9] For the crown ether complexes, we remeasured the energy-resolved CID cross sections, as has been described in our previous publications,[8] so as to obtain data under consistent experimental conditions, and then compared the CRUNCH fits to the those done with L-CID.

As is evident from Figure 4, L-CID and CRUNCH deliver virtually identical values for E_0 well within the uncertainty bounds of the measurement. For the loss of benzene from two Pt(II) complexes, shown in Figure 5, L-CID and CRUNCH again deliver very similar values for E_0 for two independent datasets. The final dataset, shown in Figure 6, displays a two-channel fit,[24] for which the agreement between L-CID and CRUNCH is acceptable.

Discussion

The value of reliable quantitative data for mechanistic arguments stands without question. Particularly in systems for which there is great structural and electronic diversity, for example, organometallic complexes in homogeneous catalysis, there is a great need for binding measurements and activation energies. Electrospray ionization tandem mass spectrometry (ESI-MS/MS) has become, in recent years, a powerful tool for investigations of organometallic reactions.[25] Ion−molecule reactions of mass-selected reactive intermediates under well-defined collision conditions give an unprecedentedly detailed look at reaction paths that are ordinarily much more difficult to see in condensed phase.[26] Most ESI-MS/MS studies of catalytic reactions have been restricted, though, to qualitative or, at best, semiquantitative experiments. Products and branching ratios are seen and compared to computed structures from DFT calculations. Despite the wealth of information available in this approach, a more meaningful and incisive test of mechanism requires quantitative data in the form of ligand binding energies as well as activation energies for reactions.

Among the various methods for quantitative, thermochemical measurements that are compatible with mass spectrometry, energy-resolved collision-induced dissociation cross-section measurements present an ideal methodological fit to ESI-MS/MS. The deconvolution of a threshold energy, E_0, from the experimental curves is conventionally done with CRUNCH, as has been thoroughly documented in the literature by Armentrout and co-workers.[10] The method, progressively elaborated since the early work on the reactions of simple metal cations in the 1980s,[11] has grown to include effects needed to handle substantially larger molecular systems, most notably the kinetic shift. This latter effect, originally proposed to rationalized breakdown curves in photoionization mass spectrometry,[14] occurs because dissociation is not observed at its thermochemical threshold, but rather at a higher energy for which the rate becomes high enough so that dissociation occurs during the finite (usually tens of microseconds) measurement window in the mass spectrometer. As the molecule becomes larger and "floppier," the difference between the thermochemical threshold and the observed threshold, the kinetic shift, increases. Although the kinetic shift is explicitly treated within CRUNCH, we nevertheless encountered both theoretical and practical limitations in CRUNCH as we moved to increasingly larger organometallic ions, which made it clear that the deconvolution procedure needed to be redone. There were improvements that could be made in the treatment of the collision event itself by applying the well-known electrostatic potential and angular momentum conservation in place of the empirical threshold function in CRUNCH. There were further improvements that could be made by applying statistical theory to the energy partitioning in the inelastic collision. The greatest improvement from the practical standpoint is, however, the implementation of a model for the density-of-states function, $\rho(E)$, which does not require an explicit calculation of all the vibrational frequencies of the energized molecule and the transition state prior to the deconvolution of the experimental cross-section data. The typical closed-shell complexes, for example, crown ether adducts of alkali metal cations, present no special problem, in principle, for electronic structure calculations, but the coordinatively unsaturated, often open-shell, complexes encountered as reactive intermediates in homogeneous catalysis are difficult to calculate with high reliability. Even after one masters the electronic structure calculation, one must obtain frequencies for the CRUNCH fit for both the energized molecule and the appropriate transition state (among many on the potential surface). The frequencies are usually harmonic, which for the flexible ligands in homogeneous catalysis, is not a very good approximation. With regard to conformational equilibria, the structurally complex ligands also usually have multiple, energetically similar conformations, each with its own set of vibrational frequencies, which would mean that a proper treatment should calculate ensemble averages for the density of states over the thermally populated conformations. In practice, such ensemble averages make very little difference, presumably because the differences in the frequencies tend to average out anyway. In the spirit of this averaging, it was decided to explore the possibility that the averaging could be taken to the extreme, the limit of a single effective frequency (combined, of course, with the number of degrees of freedom). As was discussed earlier, the reduction of canonical RRKM theory to transition state theory, as well as several isolated examples in which averaged frequencies gave promising results, suggests that the simplification could be possible.

The detailed construction, and the strategy behind the choice of methods in L-CID, has been given above or discussed in the Supporting Information. Because of the nature of the approximations, the real test of the method comes through validation with well-characterized cases, several of which having been chosen for demonstration here. The two crown ether adducts were investigated by Armentrout.[22] They are exceptionally well-behaved ions from the point of view of practical measurement, and it is possible to acquire data sets of very high quality, meaning not only reproducibility but also low experimental variance, for these ions. The crown ether adducts have been demonstrated to dissociate via a loose, orbiting transition state. The CRUNCH and L-CID fits produce very similar values for E_0; although Figure 4 does not show the CRUNCH fit superimposed on the data, the quality of the fits is similar if one compares the fit only at the onset of dissociation. L-CID successfully models the cross section over a much wider energy range, up to and including the plateau at higher energies. The convergence criterion that the variance of the fit from experiment be smaller than the summed variance of the experimental data points themselves means that there is no statistically better fit possible. L-CID was run with the choice of a loose transition state, which is indicated by the rather large values of α' that appear. It should be noted that within the ensemble of simulations with different sets of $\{E_0, \nu, \alpha'\}$ which satisfy the convergence criterion, ν can vary over ± 200 cm^{-1}, respectively, but E_0 remains confined to the narrow range of ± 0.05 eV around the cited value. The relative insensitivity of the fit to ν is understandable, given that *ratio* of the sum of states (at the transition state) to the density of states (at the energized molecule) will vary much more slowly than either the density of states or the sum of states alone, as ν is varied. In a detailed comparison, E_0 for the loss of Cs^+ from $[(18\text{-crown-}6)Cs]^+$, depicted in red in Figure 4, is found by L-CID to be 1.70 ± 0.05 eV, as compared to 1.67 eV from CRUNCH with our data and 1.74 ± 0.09 eV in the original Armentrout paper.[22] Interestingly, E_0 for the loss of Cs^+ from $[(15\text{-crown-}5)Cs]^+$, depicted in blue in Figure 4, is found by L-CID to be 1.43 ± 0.05 eV, as compared to 1.45 eV from CRUNCH with our own data. In the original Armentrout paper, this threshold was reported to be 1.04 ± 0.06 eV, although it should be noted that, in the original work, the E_0 reported for this complex was stated to be anomalously low, as indicated by comparison to computed values. A metastable isomer was postulated at the time as an ad hoc explanation for the unexpectedly low binding energies. The present measurement, for which L-CID and CRUNCH deliver virtually identical, higher, E_0 values, most likely represents the true binding energy for [(15-crown-5)Cs]$^+$.

For the loss of benzene from the two Pt(II) complexes in Figure 5, L-CID delivers results within the cited uncertainty bounds compared to our previously published work on the same system; the L-CID and CRUNCH results overlap within these same uncertainty bounds. The loss of benzene was shown in that work to proceed by a process in which the rate-determining transition state is reactant-like, early, and, therefore, tight. Qualitatively, one understands that, although the reaction superficially resembles a simple dissociation of a coordinated ligand, the reaction actually proceeds by an associative mechanism with an internal nucleophile, the chloro substituent on one of the aryl moieties, and several changes in coordination mode. Accordingly, if any of the first steps in the associative mechanism were to be rate-determining, as was suggested in our earlier work, the chosen transition state for the deconvolution of the cross-sections should be tight. The extracted fit parameters assuming a loose transition state are also given in Figure 5. Although it had been hoped that one could choose the proper transition state from the quality of fit, this hope proved to be unrealistic for both L-CID and CRUNCH. Suitable fits are obtained for both tight and loose transition states, with a difference in E_0 coming out to be about 0.5 eV, or about 12 kcal/mol, depending on the type of transition state. In our previous work, the *computed* ligand binding energy was consistent with only the tight transition state, and the conjecture was then hardened to a conclusion by a constrained scan of the potential surface along a putative reaction coordinate. In principle, this means that both L-CID and CRUNCH must rely on some auxiliary evidence outside the cross-section measurement itself to get an unambiguous E_0. The auxiliary evidence could be a quantum chemical calculation, or it could be structural, reactivity, or thermochemical data from another source.

The last set of validation data is shown in Figure 6, in which a fit is performed for a dissociation with two competing channels. The two-channel fit is more difficult for both L-CID and CRUNCH, because the simultaneous optimization of a larger number of fit parameters opens the possibility that changes in one may be compensated artifactually by changes in one of the others. The quality of the data does not allow a better fit, given that the variance between the fit and the data is smaller than the variance of the data themselves. The demands on data quality in two-channel fits are therefore higher, so with the practical limits that exist on any given instrument, it is perhaps not surprising that the absolute magnitudes for the E_0 values differ between L-CID and CRUNCH by somewhat more than they do in the single-channel cases. Nevertheless, the deviation is systematic so that the difference between E_0 for the major channel and that for the minor channel is 0.15 eV from L-CID and 0.12 eV from CRUNCH, which is very good agreement indeed.

Conclusion

Determination of ligand binding energies and activation energies for organometallic reactive intermediates involved in homogeneous catalysis is a key application for energy-resolved CID cross-section measurements in tandem mass spectrometry. Whereas the previously available program CRUNCH, designed for general use in threshold measurements, has been employed by many groups, including our own, for a variety of organometallic complexes, practical problems in the implementation for complexes with more than a few dozen atoms make the application more difficult than it needs to be. We present with this work a program, L-CID, which takes explicit advantage of the averaging that occurs when the number of degrees of freedom becomes large to deliver comparable results with much less prior input of structural or electronic state information. In practice, this means for studies of complexes with 50−100 atoms (or more) that the rate-limiting step in the work flow is no longer the data fitting, but rather data acquisition. At the level of L-CID itself, application in other areas beyond organometallic complexes can be imagined. At a lower level of the effective frequency approximation, one can imagine applications in other processes involving dissociation dynamics in a finite time window, such as blackbody infrared dissociation (BIRD) or dissociative capture experiments.

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Supporting Information Available: More detailed descriptions of the various key modules of L-CID, along with a comprehensive listing of the reference data used for construction and validation of the code. This material is available free of charge via the Internet at http://pubs.acs.org.

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