

FINDING AND VERIFYING EQUILIBRIUM AND TRANSITION-STATE GEOMETRIES

The energy of a molecule depends on its geometry. Even small changes in structure can lead to quite large changes in total energy. What is the “best” choice of geometry for use in a molecular modeling study? While experimental structures, where available, would at first glance seem to be ideal, there are multiple problems with this. First, while upwards of one million structures have been established experimentally, many, many more have not been. Second, the vast majority of experimental structures follow from X-ray crystallography on solid samples and may differ significantly from those of isolated molecules to which the calculations pertain. An additional problem with X-ray structures is that bonds to hydrogen are too short (by as much as 0.1 - 0.2Å). Finally, experimental data for reactive or otherwise short-lived molecules are scarce, and data for transition states are completely lacking. In the final analysis, there is no alternative to obtaining geometries from calculation. Fortunately, this is not difficult, although it may be demanding in terms of computer time.

Determination of geometry (geometry optimization) is an iterative process. The energy and energy gradient (first derivative of the energy with respect to all geometrical coordinates) are calculated for the initial geometry, and this information is then used to project a new geometry. This process continues until three criteria are satisfied. First, the gradient must closely approach zero. This ensures that the optimization is terminating in a flat region of the potential surface (either the bottom of an energy well in the case of equilibrium geometry or the top of an energy hill in the case of transition-state geometry). Second, successive iterations must not change any geometrical parameter by more than specified (small) value. Third, successive iterations must not change the total energy by more than a specified (small) value.

Equilibrium Geometries

In order for a geometry to correspond to an energy minimum, the curvature of the energy surface must be positive, that is, the structure must lie at the bottom of an energy well. The surface's curvature is defined by the *Hessian* (the matrix of second derivatives of the energy

with respect to geometrical coordinates).

What is actually done is to transform from the original coordinates to a new set of geometrical coordinates (*normal coordinates*) for which the Hessian will be diagonal, that is, all off-diagonal elements will be zero. In this representation, all (diagonal) elements must be positive for the geometry to correspond to an energy minimum. Normal coordinate analysis, as it is termed, is required for the calculation of vibrational frequencies, which relate directly to the square root of the elements of the (diagonal) Hessian. Positive Hessian elements yield real frequencies; negative Hessian elements yield imaginary frequencies.

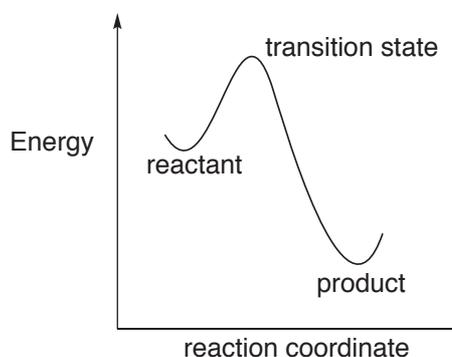
Geometry optimization does not guarantee that the final structure has a lower energy than any other structure of the same molecular formula. All that it guarantees is a *local minimum*, that is, a geometry with a lower energy than that of any similar geometry, although not necessarily the lowest energy geometry possible for the molecule. The number and types of chemical bonds are maintained in the optimization process as are single bond and flexible-ring conformers. Altering bond types would lead to isomers (stable molecules of the same molecular formula) which under normal conditions could not be reached, whereas altering conformation would lead to different “shapes” of the same molecule, which would be in equilibrium under the same conditions. Finding the best conformer or *global minimum* requires repeated optimization starting with different initial geometries corresponding to different initial conformers. Only when all local minima have been located is it possible to say with certainty that the lowest energy geometry has been identified. This process is termed *conformational analysis*.

In principle, geometry optimization carried out in the absence of symmetry, that is, with C_1 symmetry, must result in a local minimum. On the other hand, imposition of symmetry may result in a geometry that is not a local minimum. For example, optimization of ammonia constrained to a planar trigonal geometry (D_{3h} symmetry) will result in a structure that corresponds to an energy maximum in the direction of motion toward a puckered trigonal geometry (C_{3v} symmetry). This is the transition state for inversion at nitrogen in ammonia.

The most conservative tactic is always to optimize geometry in the absence of symmetry. If this is not done, it is always possible to verify that the structure located indeed corresponds to a local minimum by calculating the vibrational frequencies on the final (optimized) structure. If one or more frequencies are imaginary, then the geometry does not correspond to an energy minimum.

Transition-State Geometries

Chemists recognize a transition state as the structure that lies at the top of a potential energy surface connecting reactant and product (see the topic *Potential Energy Surfaces*).



More precisely, a transition state is a point on the potential energy surface for which the gradient is zero (just as it is for an equilibrium geometry), but for which the diagonal representation of the Hessian has one and only one negative element, corresponding to the reaction coordinate (see diagram above). All the other elements are positive. In other words, a transition state is a structure that is an energy minimum in all dimensions except one, for which it is an energy maximum. Mathematically, such a structure is referred to as a first-order saddle point.

The geometries of transition states on the pathway between reactants and products are not as easily anticipated as the equilibrium geometries of the reactants and products themselves. This is not to say that transition-state geometries do not exhibit the same systematic behavior as equilibrium geometries, but rather that there is not sufficient experience to identify what systematics do exist, and more

importantly how to capitalize on structural similarities. It needs to be recognized that transition states cannot even be detected let alone characterized experimentally, at least not directly. While measured activation energies relate to the energies of transition states above reactants, and while activation entropies and activation volumes as well as kinetic isotope effects may be interpreted in terms of transition-state structure, no experiment can actually provide direct information about the detailed geometries and/or other physical properties of transition states. Quite simply, transition states do not exist in terms of a stable population of molecules on which experimental measurements may be made. Experimental activation parameters may act as a guide, although here too it needs to be pointed out that their interpretation is in terms of *transition state theory*. This assumes that all molecules proceed over a single transition state (the high point along the reaction coordinate) on their way to products. Even then, experiments tell little about what actually transpires in going from reactants to products.

Lack of experience about “what transition states look like” is one reason why their detailed geometries are more difficult to obtain than equilibrium geometries. Other reasons include:

- i) Algorithms for locating transition states are less well developed than procedures for finding equilibrium structures. After all, minimization is an important task in many diverse fields of science and technology, whereas saddle point location has few if any important applications outside of chemistry.
- ii) It is likely that the potential energy surface in the vicinity of a transition state is more “flat” than the surface in the vicinity of a local minimum. After all, transition states represent a delicate balance of bond breaking and bond making, whereas overall bonding is maximized in equilibrium structures. As a consequence, the potential energy surface in the vicinity of a transition state is likely to be less well described in terms of a simple quadratic function (assumed in all common optimization procedures) than the surface in the vicinity of a local minimum.
- iii) To the extent that transition states incorporate partially (or completely) broken bonds, it might be anticipated that very

simple theoretical models lacking adequate treatment of electron correlation will not be able to provide entirely satisfactory descriptions.

In time, all of these problems will be overcome, and finding transition states will be as routine as finding equilibrium geometries is today. Chemists can look forward to the day when reliable tools become available for the elucidation of reaction mechanisms.

While the same iterative procedure previously described for optimization of equilibrium geometry applies as well to transition states, the number of steps required for satisfactory completion is likely to be somewhat larger. This is due to the factors discussed earlier. Note, however, that the task of transition state determination may be completely automated and needs no more human intervention than that involved in locating equilibrium geometries.

Having found a transition-state geometry, two tests need to be performed in order to verify that it actually corresponds to a proper transition state, and further that it actually corresponds to the transition state for the process of interest, that is, it smoothly connects energy minima corresponding to reactant and product:

- i) Verify that the Hessian (matrix of second energy derivatives) yields one and only one imaginary frequency. This requires that a normal mode analysis be carried out on the proposed transition-state geometry. The imaginary frequency will typically be in the range of 400-2000 cm^{-1} , quite similar to real vibrational frequencies. In the case of flexible rotors, for example, methyl groups or floppy rings, the analysis may yield one or more additional imaginary frequencies with very small ($<100 \text{ cm}^{-1}$) values. These can be difficult to “get rid of” simply because energy changes are likely to be very small and inside the precision settings of the optimization procedure. Small imaginary frequencies can almost always be ignored, but make certain to verify what motions these small imaginary frequencies actually correspond to (see discussion following) before doing so. Most important, be wary of structures that yield only very small imaginary frequencies. This suggests a very low energy

transition state, which quite likely will not correspond to the particular reaction of interest.

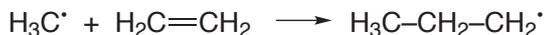
- ii) Verify that the normal coordinate corresponding to the imaginary frequency smoothly connects reactants and products. A simple way to do this which requires no additional calculations, is to animate the normal coordinate corresponding to the imaginary frequency, that is, to walk along this coordinate without any additional optimization. This does not necessarily require any additional calculations beyond the normal mode analysis already performed. “Incorrect” transition states located by calculation, that is, transition states that do not link the reactant to the expected product, may indicate new chemistry, so don’t discard them too quickly! There are more costly procedures that actually involve “walking” the geometry down from the transition state to both reactants and products. In our view these are rarely worth the effort.

Reactions Without Transition States

Not all chemical reactions have transition states, and that the rates of some reactions depend only on the speed with which reactants diffuse into one another (so-called, *diffusion controlled reactions*). In fact, reactions without energy barriers are quite common. Two radicals will typically (but not always*) combine without activation, for example, two methyl radicals to form ethane.



Radicals will often add to paired-electron species with no (or very small) activation, for example, methyl radical and ethylene forming 1-propyl radical.



Exothermic ion-molecule reactions that have activation energies in solution, do not necessarily have activation energies in the gas phase. Any complex of an ion and a neutral molecule is likely to be lower in energy than the separated species and the entire reaction coordinate for

* Exceptions may occur where both radicals are delocalized, for example, combining two benzyl radicals.

an ion-molecule reaction might lie below the energy of the separated reactants for example, nucleophilic attack by OH^- on CH_3Cl to give CH_3OH and Cl^- .

Failure to find a transition state, and location instead of what appears to be a stable intermediate or even the final product, does not necessarily mean failure of the theoretical model (nor does it rule this out). It may simply mean that there is no transition state!

Calculations Using Approximate Geometries

Given that small-basis set Hartree-Fock models, semi-empirical models and even molecular mechanics models generally provide geometries for organic molecules that are quite close to those obtained from Hartree-Fock, density functional and MP2 models, it is legitimate to ask whether or not structures from these techniques may be used as the basis for energy and property calculations.* It would be of great help were this the case as geometry optimization is a major cost in any modeling investigation.

“Exact” geometries must be used for frequency (infrared and Raman spectra) calculations. The reason for this is that frequencies are related to the first finite term in a Taylor series expansion of the energy (as a function of geometry). This is (assumed to be) the second-derivative term, which will not be true if the first-derivative term (the gradient) is not precisely zero. (Cubic and higher order terms are assumed to be small and are ignored.) Frequencies evaluated at non-equilibrium (or non-transition-state) geometries are meaningless.

* Molecular mechanics models are not applicable to transition states as they have been parameterized to account for the structures of stable molecules. This is not to say that molecular mechanics parameterizations could not be developed for transition states, simply that they have not been.