

$\theta_0)^2]$. A third class of interaction dependent on the dihedral angle ϕ between four bonded atoms is the torsional potential $\{K_\phi[1 + \cos(\phi - \delta)]\}$ used to account for orbital delocalization and to compensate for other deficiencies in the force field. A harmonic term $[\frac{1}{2}K_\xi(\xi - \xi_0)^2]$ is often introduced for dihedral angles ξ that are relatively fixed, such as those in aromatic rings. Coulomb's law $[q_i q_j / (4\pi\epsilon_0\epsilon_r r_{ij})]$ is the simplest approach to the contribution of electrostatics to the potential V :

$$V = \sum \frac{1}{2} K_b (b - b_0)^2 + \sum \frac{1}{2} K_\theta (\theta - \theta_0)^2 \\ + \sum \frac{1}{2} K_\xi (\xi - \xi_0)^2 + \sum K_\phi [1 + \cos(\phi - \delta)] \\ + \sum [C_{12}(i,j)/r_{ij}^{12} - C_6(i,j)/r_{ij}^6] \\ + \sum q_i q_j / (4\pi\epsilon_0\epsilon_r r_{ij}).$$

A central issue is the number of different atom types that are used in a particular force field. There is always a compromise between increasing the number to allow for the inclusion of more environmental effects (i.e., local electronic interactions) vs. the increase in the number of parameters to be determined to adequately represent a new atom type. In general, the more subtypes of atoms (how many different kinds of nitrogen, for example), the less likely that the parameters for a particular application will be available in the force field. The extreme, of course, would be a special atom type for each kind of atomic environment in which the parameters were chosen, so that the calculated properties of each molecule would simply reproduce the experimental observations. One major assumption, therefore, is that the force constants (parameters) and equilibrium values of the equations are functions of a limited number of atom types and can be transferred from one molecular environment to another. This assumption holds reasonably well where one may be primarily interested in geometric issues, but is not so valid in molecular spectroscopy. This had led to the introduction of additional equations, the so-called "cross-terms" which allow additional parameters to account for correlations between bond lengths and bond angles $[K_{b\theta}(b$

$- b_0)(\theta - \theta_0)]$, dihedral angles and bond angles, and so forth. Because of the lack of adequate parameterization of the more complex force fields that are usually specialized to one kind of molecule (e.g., proteins or nucleic acids), more simplified force fields have gained some popularity because of their general applicability, despite limited accuracy.

Examples are the Tripos force field (22), the COSMIC force field (23), and that of White and Bovill (24), which uses only two atom types, those at the end of the bond to parameterize the torsional potential rather than the four types of the atoms used to define the torsional angle. One has only to consider the number of combinations of 20 atom subtypes taken four at a time (160,000) versus two at a time (400) to understand the explosion of parameters that occurs with increased atom subtypes. The simplifying assumption in parameterization of the torsional potential reduces to some extent the quality of the results (25), but allows the use of the simplified force fields (22) in many situations where other force fields would lack appropriate parameters. The situation can become complicated, however. For example, the amide bond is normally represented by one set of parameters, whether the configuration is *cis* or *trans*. Experimental data are quite compelling that the electronic state is different between the two configurations, and different parameter sets should be used for accurate results (Fig. 3.1). Only AMBER/OPLS currently distinguishes between these two conformational states (26). Certainly, the limited parameterization of simplified force fields would not allow accurate prediction of spectra that is more reflective of the dynamic behavior of the molecule.

Accurate estimates of energy may require accurate representation of the dynamics of molecules and justify derivation of the larger number of parameters. The new version (27) of the Allinger force field, MM3, has the objective of reproducing spectral data more accurately than MM2. Much of the chemistry remains to be incorporated into appropriate force fields. Only recently have adequate modifications been made to the force fields developed for organic molecules to include some metals (28–31). Carlsson (32, 33) recently de-