Table 8.3.2.3. *Typical values of standard deviations for use in determining weights in restrained refinement of protein structures (after Hendrickson, 1985)*

Interatomic distances		
Nearest neighbour (bond)		σ_d = 0.02 Å
Next-nearest neighbour (angle)		0.03 Å
Intraplanar distance		0.05 Å
Hydrogen bond or metal coordination		0.05 Å
Planar groups		
Deviation from plane		σ_p = 0.02 Å
Chiral centres		
Chiral volume		σ_c = 0.15 Å^3
Nonbonded contacts		
Interatomic distance		σ_n = 0.50 Å
Torsion angles		
Specified (*e.g.* helix φ and ψ)		σ_t = 15°
Planar group		3°
Staggered		15°
Thermal parameters	Anisotropic	Isotropic
Main-chain neighbour	σ_v = 0.05 Å	σ_B = 1.0 Å^2
Main-chain second neighbour	0.10 Å	1.5 Å^2
Side-chain neighbour	0.05 Å	1.5 Å^2
Side-chain second neighbour	0.10 Å	2.0 Å^2

commonly found in proteins. The ideal conformations of pairs of amino acid residues, from which the ideal values to be used in restraint terms of various types may be determined, are constructed by combining the coordinates of the individual groups. For example, consider a dipeptide composed of glycine and alanine joined by a *trans* peptide link, giving the molecule

$$\begin{array}{ccccccccc} & & & & O(1) & & C\beta(2) & O(2) & \\ & & & & \| & & | & \| & \\ N(1)\text{—}C\alpha(1)\text{—} & & & & C(1) & \text{—}N(2)\text{—} & C\alpha(2) & \text{—}C(2) & \text{—}O_t(2). \end{array}$$

The origin is placed at each of the Cα positions in turn, and interatomic distances to nearest and next-nearest neighbours are computed. Planar groups and possible nonbonded contacts are identified, and torsion angles and chiral volumes for chiral centres are computed. Table 8.3.2.2 is a summary of the restraint information for this simple molecule. In order to incorporate this information in the refinement, these ideal values are combined with suitable weights. Table 8.3.2.3 gives values of the standard deviations of the various types of constraint relation that have been found (Hendrickson, 1985) to give good results in practice.

Even for a small protein, the normal-equations matrix may contain several million elements. When stereochemical restraint relations are used, however, the matrix elements are not equally important, and many may be neglected. Convergence and stability properties can be preserved when only those elements that are different from zero for the stereochemical restraint information are retained. The number of these elements increases linearly with the number of atoms, and is typically less than 1% of the total in the matrix, so that sparse-matrix methods (Section 8.1.5) can be used. The method of conjugate gradients (Hestenes & Stiefel, 1952; Konnert, 1976; Rae, 1978) is particularly suitable for the efficient use of restrained-parameter least squares.

references