and the activity coefficient has been estimated for binary regular solutions involving a liquid solute. Rearranging the equation to the form:

$$\ln \gamma_2 = \frac{\bar{V}_2 \phi_1^2}{RT}\left(\delta_1 - \delta_2\right)^2 \tag{2.42}$$

allows inclusion of this term in Equation 2.32 to define the regular solution equation for a crystalline solute:

$$\ln X_2 = -\frac{\Delta \bar{H}_f}{RT_m}\left(\frac{T_m - T}{T}\right) - \frac{\bar{V}_2 \phi_1^2}{RT}\left(\delta_1 - \delta_2\right)^2 \tag{2.43}$$

It should be noted that $\bar{V}_2$ actually represents the partial molal volume of the liquid form of the solute at the solution temperature, and not the molar volume of the liquid. If the solution temperature is below the melting point of the solute, $\bar{V}_2$ would be estimated by the molar volume of a supercooled liquid form of the solute at temperature, *T*.

Equation 2.41 would be useful if the values of the solubility parameters and the partial molal volume of the supercooled liquid solute could be estimated. Additive procedures, based on functional groups found in the molecule, have been developed to estimate partial molal volumes and solubility parameters (Small, 1951; Hoy, 1970; Konstam and Feairheller, 1970; Fedors, 1974). Rathi (2010) presents the calculation of the Hildebrand solubility parameter for satranidazole (Consider Figure 2.2, Table 2.1) based on the group contribution values offered by Fedors (1974). Each functional group in the chemical is acknowledged not only by type but also by the number of times that functional group appears. The features of the chemical structure are also included, such as each time conjugation appears (represented by a series of double then single bonds) and each ring closure (such as the *N*-methyl imidazole ring). In Table 2.1, the sum of the entries in column D equals the estimated contributions to the cohesive energy density of satranidazole; the sum of the entries in column F equals the estimated molar volume of the supercooled liquid form of satranidazole at room temperature. The cohesive energy density for satranidazole therefore equals the sum of column D divided by the sum of column F that leads to:

$$\text{Satranidazole solubility parameter}, \delta = \sqrt{\frac{30580 \text{ cal/mole}}{235.6 \text{ cm}^3\text{/mole}}} = 11.4\sqrt{\frac{\text{cal}}{\text{cm}^3}}$$

Another approach is to determine the solubility of the compound in a series of nonpolar solvents and use Equation 2.43 to estimate the solubility parameter of the solute by accounting for every other parameter in the equation. This has been somewhat successful for hydrocortisone (Hagen and Flynn, 1983) and for para-aminobenzoates (Neau et al., 1989). A plot of $\ln X_2$ as a function of the solubility parameter of the solvent, according to Equation 2.43, reveals a parabola for solubility data in reasonably nonpolar solvents (Figure 2.3). The maximum for the parabola occurs when the solvent solubility parameter equals the solute solubility parameter and the maximum represents the ideal solubility, as defined by Equation 2.15 or 2.29. It was shown that, by choosing a nonpolar solvent with a solubility parameter reasonably removed from that calculated for the solute, such as *n*-hexane ($\delta_1 = 7.27$) or:

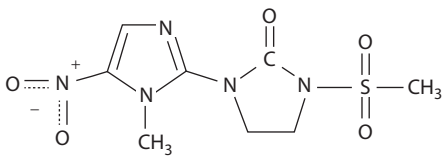

FIGURE 2.2 Chemical structure of satranidazole.