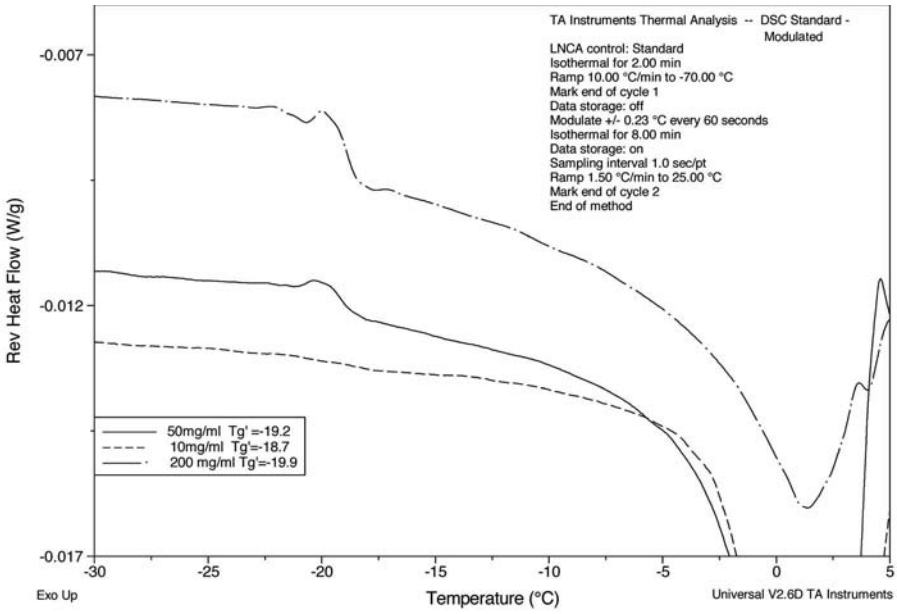

FIGURE 11 Modulated DSC profile of heparin run at three different concentrations showing amplitude of the T_g' response with concentration [run on 2920 DSC (TA Instruments, Crawley, U.K.)] at 1.5°C/min, 0.23°C/min modulation in steel high-volume pans.

The limitations of this methodology are that some samples (e.g., plasma and albumin) appear to give no glass transition, even at high concentration (10–20% wt/vol protein), and often the standards to be dried are only available in small quantities and dilute concentration making T_g' determination by mDSC difficult. For example, in our experience no specific T_g' was detectable by DSC for a preparation of tRNA at 1 mg/mL. In the literature, a value for modified RNA was reported using DSC (25) but with analysis on a sample at 100-mg/mL concentration—conditions that would be unlikely to be available for most nucleic acid samples we encounter. In other samples containing sodium chloride the T_{eu} event dominates the profile and weak T_g' may be missed or masked.

In summary, DSC is a rapid technique and can be automated but requires a significant financial outlay for the equipment and does not provide T_g' values for all samples under consideration for freeze-drying. However, it offers the advantage of also allowing the determination of the T_g of the dried state that may be of benefit when studying formulation selection and storage stability (see chap. 8).

Electrical Resistance

The changes in electrical resistance that occur as a sample undergoes incipient melting can be followed by a number of methods (26). At NIBSC the SLTT—solid-liquid transition temperature—was measured for many years [using an in-house technique, performed with equipment developed in conjunction with