these two figures, we conclude that glycine was indeed crystallized when the annealing step was incorporated into the freezing cycle as observed by the sharp peaks in the diffractogram at the specific angles corresponding to standard crystalline glycine.

In addition to DSC, other instruments, such as DTA and electrical resistance analysis (ERA), are also commonly used in determining the thermophysical properties of a lyophilized formulation, such as the glass transition temperature, the collapse temperature, etc. One of the examples using DTA and ER has been recently reported by Ma et al. on a similar crystalline matrix formulation (14). Other literature on the application of DTA (16–18) and ER (3,16,17, 19–21) in formulation characterization is also very informative. However, DSC is the most common and reliable means, and also the easiest.

CONFIRM DSC RESULTS WITH A FREEZE-DRYING MICROSCOPE

A freeze-drying microscope provides real-time images of freezing, melting, crystallization, collapse, and melt-back during the freezing and lyophilization processes. A freeze-drying microscope that we have in our laboratory is shown in Figure 5, consisting of two major parts, an optical microscope with a Physitemp FDC-1 freeze-drying microscope stage. To investigate the freeze-drying behavior of the crystalline matrix formulation described previously, a small aliquot (10 μL) of formulation was frozen to −48°C between quartz coverslips in the freeze-drying stage, either with or without annealing. The behavior of the material during sublimation drying was then observed at temperatures between −48°C and −11°C using an Olympus BX50P polarizing microscope. Micrographs were recorded using a Javelin Smartcam CCD video camera mounted on the microscope and a Data Translation DT3153 frame grabber card. The magnification used for observation of the freeze-drying front was 150×. More details about this type of freeze-drying microscope can be found in Nail (9). Studies of freeze-drying microscopy have also been reported by others (3,4,18, 22–24).

FIGURE 5 A freeze-drying microscope.