

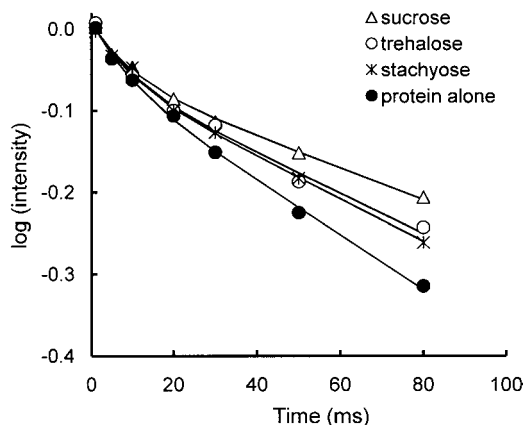
insulin carbonyl carbon in the insulin-trehalose system is longer than in the insulin-dextran system, indicating that the molecular mobility of insulin is decreased by trehalose, since longer  $T_{1\rho}$  indicates slower motion in the slow motional regime (Fig. 3).

Retardation of spin-lattice relaxation of protein carbonyl carbon brought about by the addition of sugars is also observed for the carbonyl carbon of  $\beta$ -galactosidase freeze-dried with sucrose, trehalose, or stachyose, as shown in Figure 11 (33). The molecular mobility of the protein is most effectively decreased by sucrose.

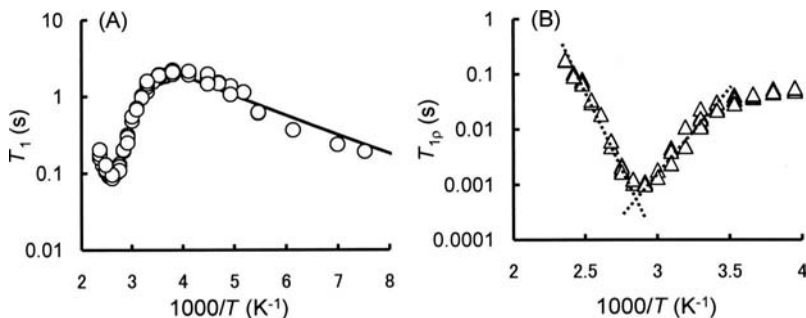
The  $T_1$  and  $T_{1\rho}$  of protein carbonyl carbon described above represent the average of  $T_1$  and  $T_{1\rho}$  for multiple carbonyl carbons present in the protein molecule. More detailed site-specific analysis becomes possible by the  $^{13}\text{C}$ -labeling of an amino acid at a specific site of interest.

### Laboratory and Rotating Frame Spin-Lattice Relaxation Times of Fluorine

$^{19}\text{F}$ -NMR has high sensitivity and specificity and has been used to determine the molecular mobility of  $^{19}\text{F}$ -labeled proteins (34) as well as small molecules containing  $^{19}\text{F}$  (35). Figure 12 shows the temperature dependence of  $T_1$  and  $T_{1\rho}$  of



**FIGURE 11** Time course of spin-lattice relaxation for carbonyl carbon of  $\beta$ -galactosidase freeze-dried with sucrose, trehalose, or stachyose at  $25^\circ\text{C}$  and 12% RH.



**FIGURE 12** Temperature dependence of  $T_1$  (A) and  $T_{1\rho}$  (B) of flufenamic acid  $^{19}\text{F}$  in solid dispersions with PVP. Abbreviation: PVP, polyvinylpyrrolidone.