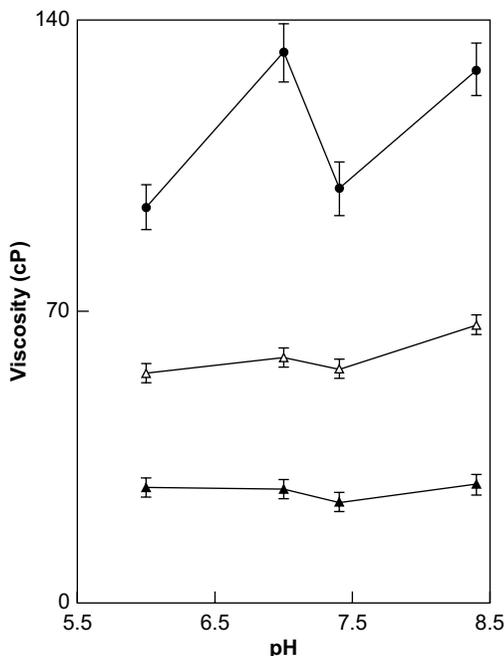**Figure 7.9** The pH-dependence of the viscosity of a 300 mg/mL γ-globulin solution with no excipient added (solid circles) or in the presence of 0.5 M NaI (open triangles) or 0.5 M trimethylphenylammonium iodide (solid triangles). From Du and Klibanov (2011).

(Arakawa et al., 2007; Inoue et al., 2014). An important use of ArgHCl in reducing viscosity is for an IgG1 mAb where the ideal pH of the liquid formulation was 6.0 where the rates of Asp isomerization and deamidation are minimized as discussed previously (Figure 4.3). However, at pH 6 the viscosity of this IgG1 mAb at 130 mg/mL is at a maximum (Figure 7.10). Thus, a formulation that stabilizes chemical degradations also results in a maximum viscosity. Using an ArgHCl histidine buffer system at pH 6 effectively reduced the viscosity from about 80 to 13 mPa s while maintaining the optimization of the chemical degradations (Figure 7.10). Although ArgHCl appears to have wide applicability for dealing with PPI and viscosity, it does not always work effectively. An IgG$_4$ mAb (with a mutation at the hinge region that makes it more like an IgG$_1$ mAb preventing the half molecule formation often seen with IgG4) was formulated with and without arginine salts. The rate of aggregation was substantially greater in the presence of arginine succinate at pH 5.5 and the viscosity was essentially unaltered when formulated with arginine acetate at pH 5.5 (Figure 7.11). Since these studies were not conducted with ArgHCl, it leaves open the question of the role of the counterion, but certainly shows that arginine may not always be effective in reducing viscosity of a mAb.

Another approach to lowering viscosity is to formulate mAbs at lower concentrations since the viscosity varies exponentially with concentration (Figure 6.1). However, such an approach requires the SC administration of large volumes to attain similar dosing at the higher concentrations. Until now excipients have been chosen based on their ability to reduce attractive interactions and lower viscosity of the