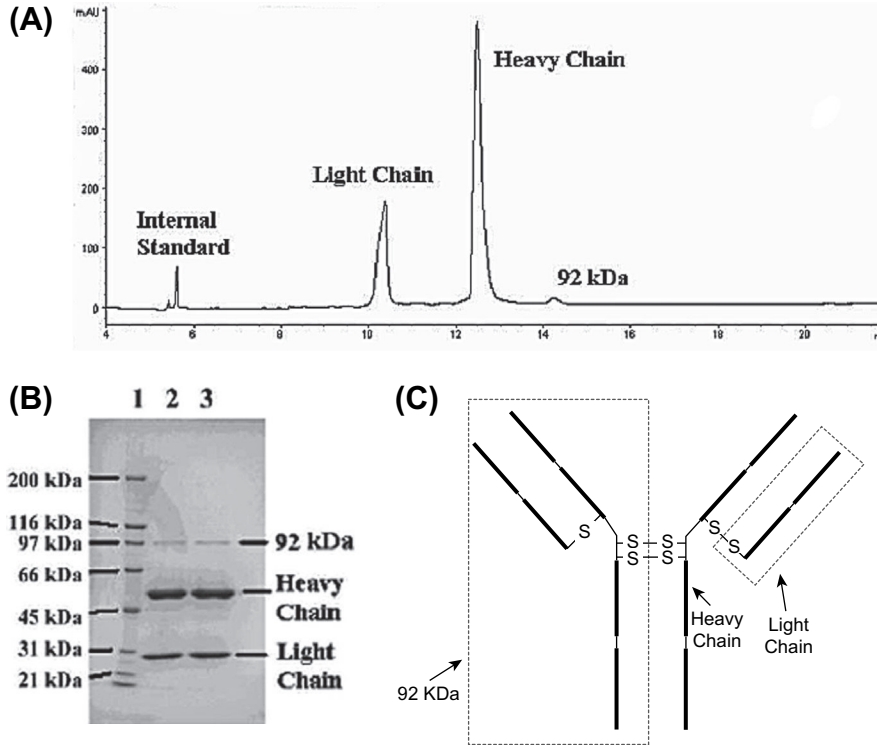

Figure 3.16 Generation of a 92 kDa thioester cross-link between the heavy and light chain in a humanized mAb. (A) Reducing capillary gel electrophoresis, (B) SDS PAGE, lane 1—molecular weight standards, lanes 2 and 3 reduced. (C) Schematic of the heavy chain, light chain, and 92 kDa cross-linked species.
Reproduced from Tous et al. (2005).

storage. Nonreducible thioether cross-links were also observed in several antibodies by size exclusion chromatography coupled with a mass spectrometer detector (Liu, Gaza-Bulseco, & Chumsae, 2009). It has been proposed that the β-elimination mechanism for a disulfide bond creates a cross-link of Cys with dehydroalanine that leads to the generation of a thioester linkage (Galande, Trent, & Spatola, 2003; Liu & May, 2012).

Physical degradation

Many chemical degradation pathways can lead to physical alterations of a protein and this has been discussed in the previous section. Here we consider physical degradation that is not driven by covalent modifications of primary structure. There are essentially three areas of interest: conformational changes, aggregation, and surface adsorption. This will now be discussed in general for protein biotherapeutics with an emphasis on mAbs.