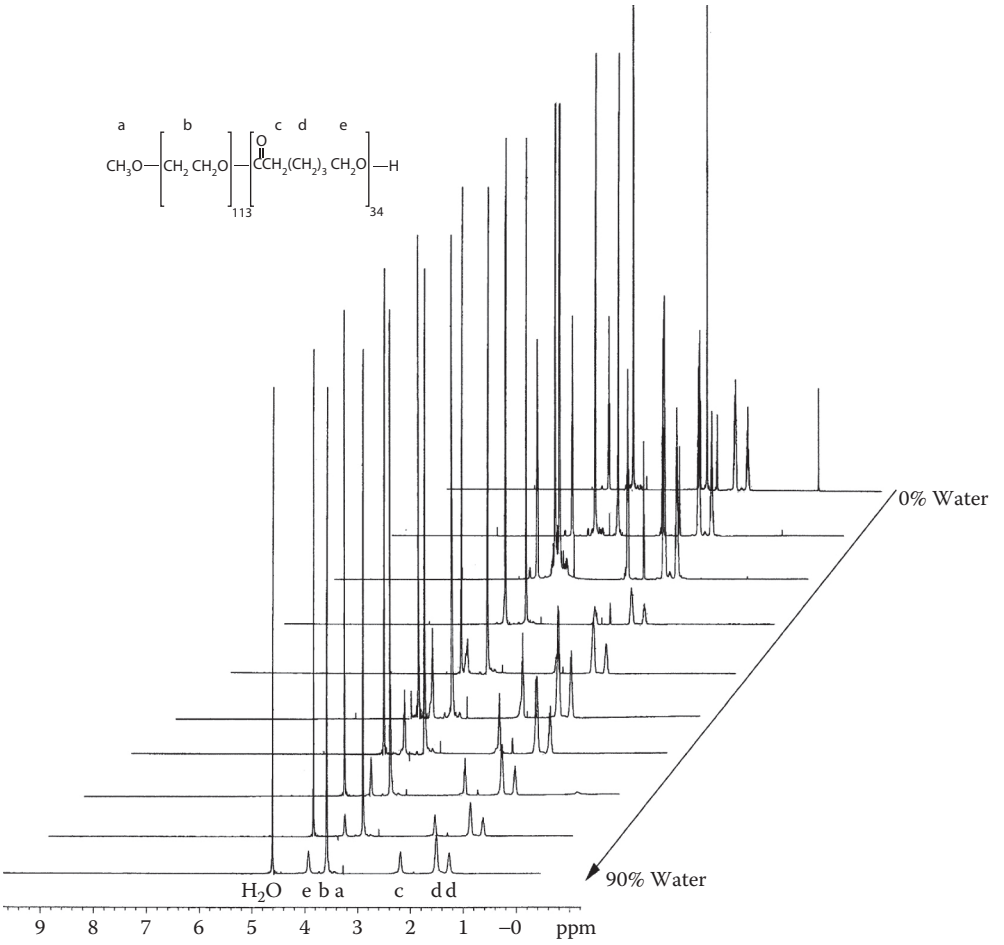

FIGURE 13.21 1H-NMR spectra of PEG-*b*-PCL (5000:4000 MW) in ACN-d_3 with gradual addition of D_2O to 10% D_2O (v/v). (With kind permission from Springer Science+Business Media: *Pharm. Res.*, Preparation and drug loading of poly(ethylene glycol)-block-poly(ε-caprolactone) micelles through the evaporation of a cosolvent azeotrope, 21, 2004, 1184–1191, Jette, K.K. et al.)

the water fraction increased to ca. 40%, there was sharp collapse into 20–60 nm monodisperse micelles. At the CWC, the ^{1}H-NMR (D_2O/ACN-d_3) resonances of the PCL block groups broadened and diminished in intensity, whereas the PEG ethylene resonance was unchanged (Figure 13.21).

Flash Nanoprecipitation

The flash nanoprecipitation technique is a variation of cosolvent extraction, wherein the micelle unimers and drug are dissolved in a volatile water-miscible organic solvent and then added to an agitated aqueous nonsolvent, that is, water or buffer solution. On addition to the aqueous nonsolvent, the unimers and drug are in a supersaturated state and spontaneously nucleate into nanoaggregates on the ms time scale (ca. 10 ms). The aggregates fuse until steric hindrance of the brush, that is, the hydrated PEO block, prevents rapid uniner exchange, kinetically freezing the micelle (Johnson and Prud'homme, 2003a). Johnson and Prud'homme (2003b) have provided a detailed study on the scale-up of flash nanoprecipitation to large production levels.

Ge et al. (2002) prepared triblock copolymer micelles of PCL-*b*-PEO-*b*-PCL encapsulating nimodipine by flash nanoprecipitation. The PCL-*b*-PEO-*b*-PCL copolymer, 100 mg, and nimodipine,