

# Protein folding in the protic ionic liquid milieu: from native conformation to fibril.

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**Abstract** Protic ionic liquids (pILs) stand as a versatile subclass of the ionic liquid family. They are low melting (<100°C) liquids formed by neutralization of a Brønsted acid by a Brønsted base, and consist only of ions. Despite the absence of water, pILs have an acidity (an “effective pH”) lying between those of acid and base components. We describe NMR methods of calibrating the acidity (or “proton activity” PA) of a given solvent, and we use composition control of the PA to create media that can either stabilize or destabilize the proteins we study. Here we show how PA tuning can stabilize the native state of simple globular proteins, like hen egg white lysozyme, to concentrations as high as 350 mg/ml, but can also destabilize it so that it forms amyloid fibrils. Finally we report that, using pILs, the native state can be reformed with most of its original bioactivity.