In continuous isothermal titration calorimetry, binding between a ligand and receptor molecule is studied by slowly and continuously titrating one reactant into the other. This is in contrast to the more common approach of incrementally adding small aliquots of titrant in discrete steps. There are two advantages to the continuous titration approach: a continuous record of the heat of binding is obtained, providing a large number of data points for fitting binding models, and data acquisition is rapid, allowing a full data set to be collected in the time normally required for just several incremental injections. Continuous titration calorimetry has been an established technique since the 1960s (Izatt et al., 1966) but is less commonly used than ITC. We have recently shown that adapting a CSC ITC instrument to continuous titration requires no changes to the data collection software and only minor changes to the data analysis software. Precise continuous delivery of titrant (from 0.05 to 0.15 µL/sec) using the Nano-ITC III instrument allows both weak (barium chloride binding to 18-crown-6) and tight (2'-CMP binding to RNase A) binding reactions to be characterized in less than 20 minutes. Data are collected at one point/second; single raw, unsmoothed data sets are shown. Results for the barium chloride titration into 18-crown-6 are in agreement with literature values (Ziemer et al., 2005), and the 2'-CMP titration into RNase A results are consistent with the literature (Wiseman et al., 1989) for these experimental conditions.

In a single continuous titration experiment, the Nano-ITC III provides rapid, accurate measurements of stoichiometry, binding constant and enthalpy for reactions with millimolar or micromolar binding constants.

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