TABLE 4.6 (*Continued*)

Equipment Available for Sirius for pK_a, Log *P*, and Solubility Measurement and Data Handling

Instrument	Features
GLpH: automated pH measurement	• High degree of accuracy • Easy to use • Automatic calibration and reminders • Available in single-sample or autosampler versions • One-button operation for most measurements • built-in GLP • "Normal" and "supervisor" access modes
RefinementPro2: automatic clipping of data	• Automatic selection of reference ranges for D-PAS assay • Dataset quality marker • Improved "Approx" function with Auto-Bjerrum analysis • GLpK_a /D-PAS to be used with a laptop • Turbidity sensing with D-PAS probe (optional) • Assay planner (optional) • Autorefinement of pH-metric and D-PAS data
CheqSol: solubility on GLpK_a, with results in less than 1 hour	• Equilibrium and kinetic result • Sample does not require chromophore • Result confirmed within same experiment • Most samples measured without cosolvent • No filtration or separation required • No need to speculate whether sample is at equilibrium • Wide measurement range
Fast D-PAS: pK_a values in just 4 minutes	• Fast D-PAS is a new way to measure pK_a values • It combines the power of UV spectroscopy with the flexibility of pH-metric titration • Gains speed by titrating in the presence of a unique linear buffer solution • Fast D-PAS assays take about 4 minutes, including the time required to fill • Dispensers, move probes, titrate, read spectra, and clean up after assay

Source: From http://www.sirius-ai.com/index.htm.

Note: Aqueous titrations using Sirius instruments is the easiest method for pK_a and log *P* measurements and provides detailed information on the partitioning characteristics of a sample at all pH values. The PCA200 and GLpK_a and pK_a/log *P* analyzers are based on a potentiometric titration method. The basic principle of operation is to determine the pK_a by titration followed by a back titration to determine the apparent pK_a in the presence of octanol. Any partitioning by the compound will shift the equilibrium and cause a change in the apparent pK_a. From this shift, the log *P* may be calculated. Sophisticated software allows detailed iterative calculations to be made and values to be carefully refined. If a sample is soluble, then it is possible to determine all its pK_a values, its log *P*, and the apparent log *P* at every pH. In addition, log *P* values of ionized species where they occur may also be calculated. The technique can be performed on samples at a concentration of 0.0001 M or above, the ideal concentration being 0.0005 M. Using the PCA200 for a suitable molecule, the analysis time would be a few hours, including calculation time. The GLpK_a has an autosampler and can also do multiple titrations on each sample. If the sample is highly insoluble, then the log *P* cannot be measured. The pK_a can be measured by either partial titration or by a Yesuda–Shedlovsky experiment where three titrations in aqueous methanol are performed, each with a different proportion of methanol. From the results, a corrected extrapolation gives the theoretical aqueous value; the technique can be performed on samples at a concentration of 0.0005 M (6).

Abbreviations: CheqSol, chasing equilibrium solubility; UV, ultraviolet.