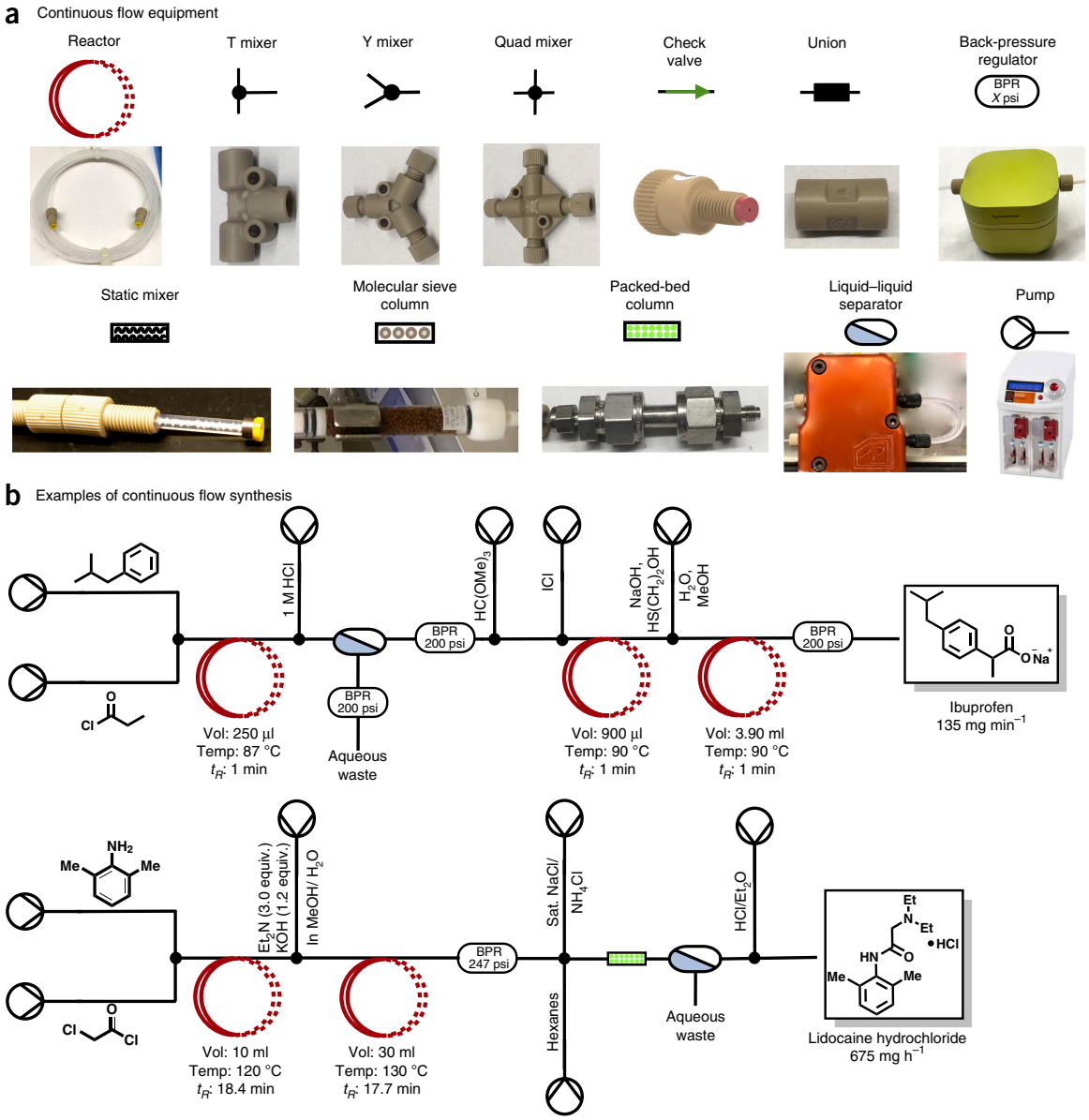

Figure 1 | Continuous flow equipment and its use in the multistep continuous flow synthesis of active pharmaceutical ingredients. (**a**) Typical equipment used in the assembly of the continuous flow systems that are discussed in this protocol. (**b**) Multistep continuous flow syntheses of ibuprofen and lidocaine hydrochloride, as published by our laboratory[37,36]. BPR, back pressure regulator; sat., saturation; *tR*, residence time of the fluid in the system.

Development of the protocol

We maintain that a continuous flow apparatus should be (i) modular, so that it can be easily replaced to create a variety of systems, (ii) quick to assemble from readily available and cost-effective parts, and (iii) easy to operate, allowing both new and experienced researchers to harness the benefits of continuous flow chemistry. For example, the synthesis of lidocaine hydrochloride requires assembly of multiple syringes, pumps, reactor coils, a back-pressure regulator, and an in-line liquid–liquid separator (**Fig. 1b**). To then synthesize ibuprofen, users need only re-arrange the syringe pumps, add a new reactor coil, and then exchange a static mixer for a back-pressure regulator. This whole process takes ~30 min and allows the synthesis of another API.

To advance this concept, modular continuous flow equipment has been developed that is readily assembled from affordable and commercially available components, allowing researchers to explore continuous flow synthesis without purchasing expensive equipment. In addition, the synthesis of APIs and commodity chemicals such as ibuprofen[36], lidocaine hydrochloride[37], diphenhydramine hydrochloride[37,38], diazepam[37], fluoxetine hydrochloride[37], atropine[39], rufinamide[40], aliskiren[41,42], and AS-136A (ref. 43) has been achieved (**Fig. 1b**). Furthermore, fluorination using SF_6 (ref. 44), biocatalysis[45], controlled polymer growth[46], and a range of synthetic transformations has been mediated by 'in-lab'-constructed systems[16,47–57].

As with traditional organic synthesis, a range of accessories is required for continuous flow synthesis. Typically, systems are operated with a back-pressure regulator to ensure fluid homogeneity as it proceeds through the reactor; if there is no back pressure, then the liquid passes through the reactor too quickly