



**FIGURE 2.** Flowchart for cross-linking screening. This scheme depicts a general method of screening cross-linkers for potential target proteins and illustrates the variables that must be considered to achieve positive outcomes (*solid arrows*) in the selection of a suitable cross-linker. The paths indicated by the dotted arrows illustrate the empirical nature of the cross-linking approach. For example, if a desired conjugate is not detected after incubating the target proteins with a large excess of the cross-linker being tested, then either different conditions of cross-linking (pH, time, protein concentration, etc.) must be tested, or a new cross-linker with different chemistries must be evaluated.