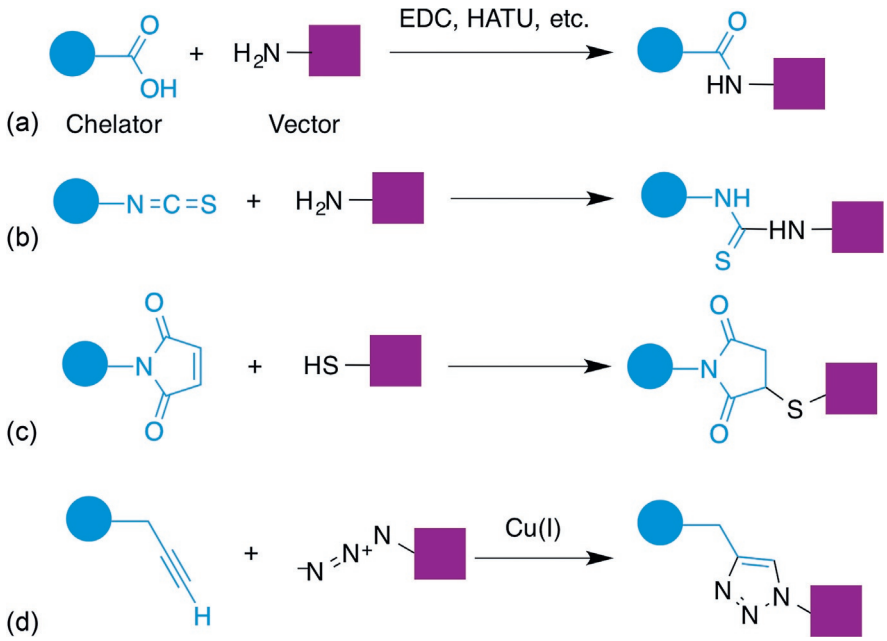

FIGURE 4.46

Main bioconjugation strategies for attaching chelator moieties to the biological vector.

Four major bioconjugation strategies are employed for attaching the chelator to the biological vector (Figure 4.46):

1. Peptide bond formation, which involves coupling one or more of the many carboxylic groups of the chelator to an amino group of the vector, using one of the many well-known coupling reagents employed in peptide synthesis (EDC, HATU, HOBt, etc.).
2. Thiourea formation, from nucleophilic addition of an amino group of the vector to an isocyanate in the chelator.
3. Thioether formation, from Michael addition of a thiol group from a cysteine in the peptide or protein acting as a vector and a maleimide unit in the chelator.
4. Use of the "click" reaction—that is, a Cu(I)-catalyzed Huisgens [3+2] dipolar cycloaddition between a terminal alkyne and an azide. The electron-rich nitrogen atoms of the resulting triazole ring may contribute to chelation.

The biological half-life of the vector must be adjusted to the radioactive half-life of the nuclide. In general, antibodies, which require long times to accumulate at the tumor site, are best matched to isotopes with long half-lives, whereas peptides are more suitable for short half-life isotopes. There are several radiolabeled monoclonal antibodies marketed for cancer therapy, including Bexxar® (^{131}I), Zevalin® (^{90}Y-labeled ibritumomab tiuxetan), and ProstaScintas® (^{111}In capromab pendetide),