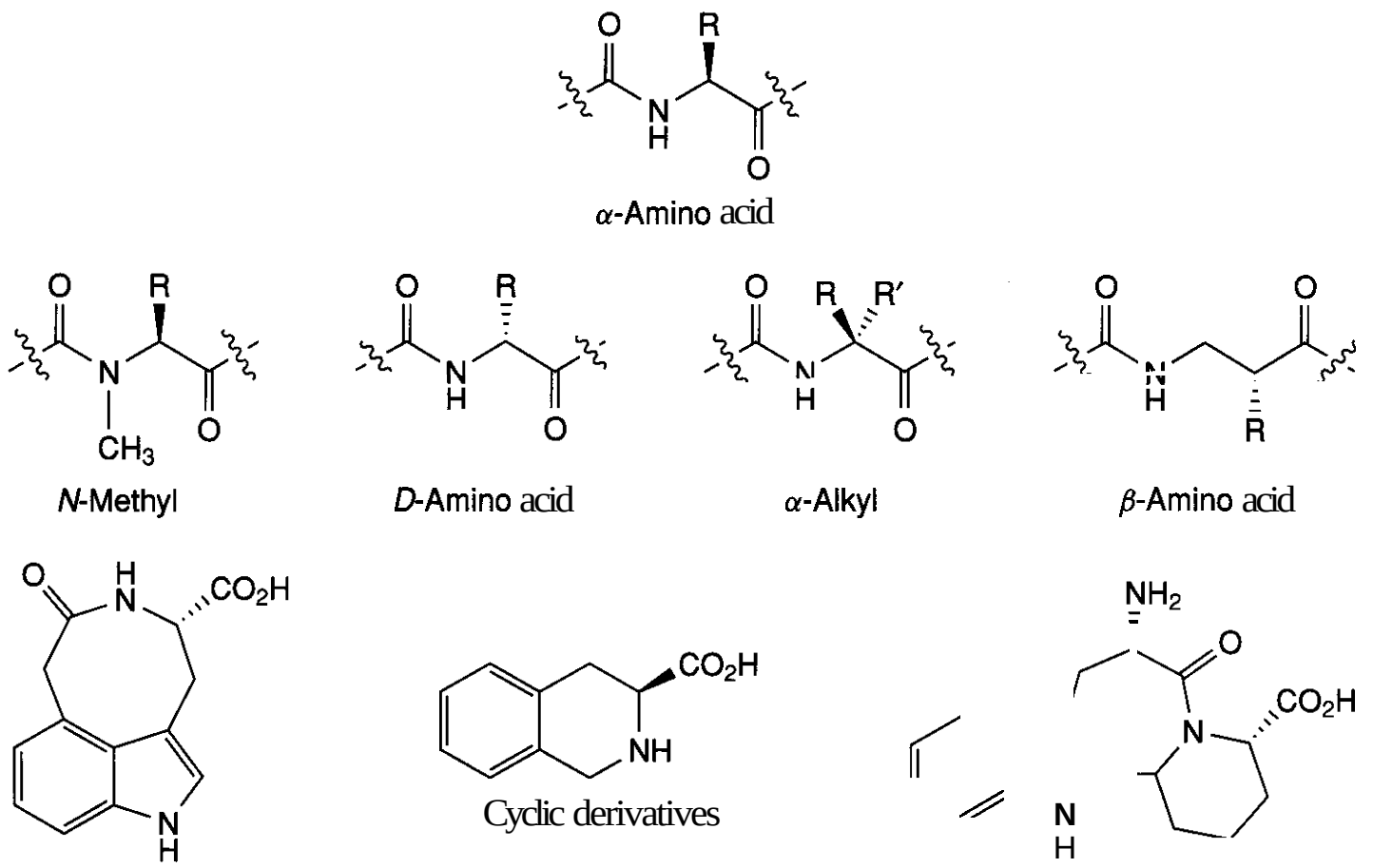


**Figure 15.7.** Representative amino acid mimetics.

have been found that efficiently mimic turns, strands, sheets, and helices. By far, the major efforts have focused on the design of β-turn mimetic~Some of the templates used to constrain the conformational torsion angles of the peptide chain are summarized in Figs. 15.8–15.14.

In a very early example, Freidinger et al. developed a series of cyclic lactams that stabilized β- and γ-turn structures in linear peptides (Fig. 15.8). This strategy was applied to determine conformations of LH-RH that are consistent with the turn structure permitted by the constraint. For example, the 3-aminolactam (18)was used to mimic a p-turn conformation. When inserted in LH-RH, compound (19) retained good biological activity so that the bioactive conformation of LH-RH probably contains a β-turn around residues 6 and 7 (48).

Conformational restriction has also been used to determine the bioactive conformation of enzyme-inhibitor systems for which no X-ray crystal structure is available. Thorsett et al. (49) synthesized conformationally restricted bicyclic lactam derivatives of the angiotensin converting enzyme (ACE)inhibitors enalapril (20) and enalaprilat (21) (Fig. 15.9) to characterize torsion angles in the bioactive conformation. Analog (22) was used to constrain the torsion angle psi (Ψ). Flynn et al.

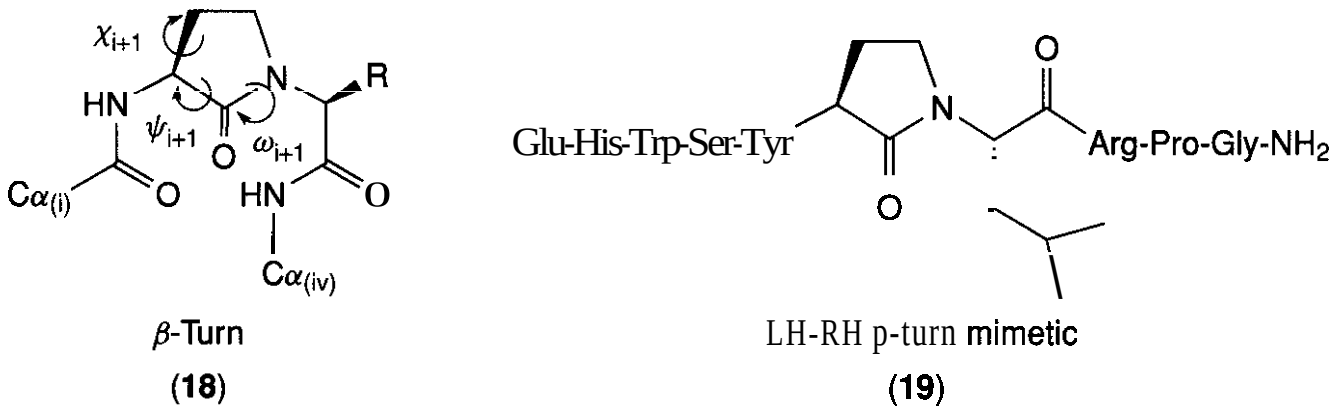


**Figure 15.8.** γ-Lactam analog of LH-RH. A β-turn mimetic.