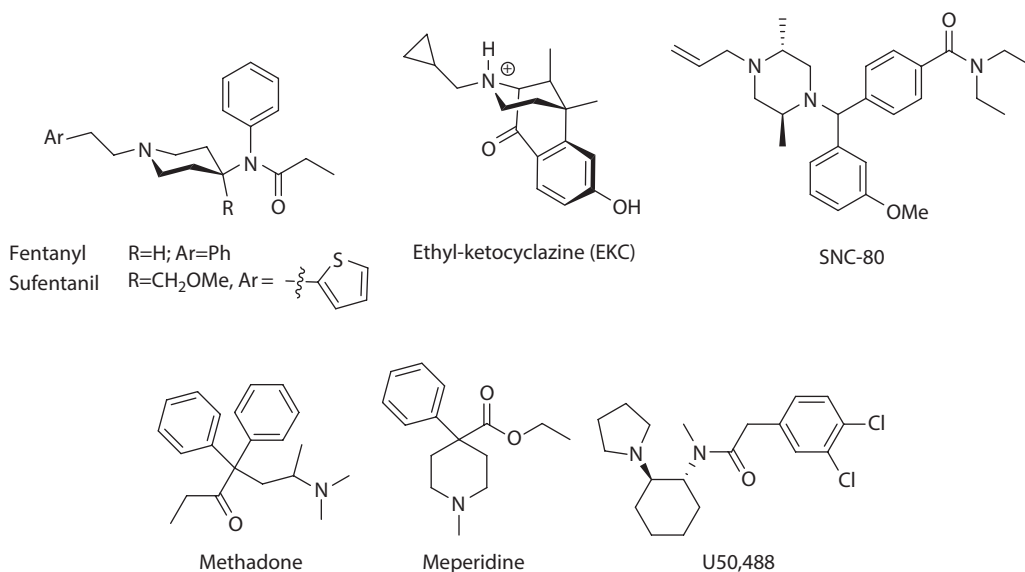


**FIGURE 19.4** The message-address concept of the development of opiates is shown schematically in the box. The message region defines the activity of the compounds, whereas the address region defines the selectivity of the compounds. The structural development in the progressive simplification of the morphine scaffold via morphinans and benzomorphans to piperidines, and also via benzazocines, spiropiperidines to piperidines and phenylpropylamines.



**FIGURE 19.5** Examples of different structural classes of opioid receptor ligands.

with a spacer of optimal length that would exhibit a potency that is greater than that derived from the sum of its two monovalent pharmacophores. This would provide evidence that the receptors existed as dimers. One of the first series were compounds **19.1** (Figure 19.6,  $n = 0, 2, 4, 6, 8$ ) dimerizing a naltrexone analog. The optimal spacer length was shown to be  $n = 4$  giving the highest activity.