and it is this form that is stabilized by competitive antagonists (Figure 4.12). When glutamate or an agonist binds to the ligand-binding domain, a change in conformation occurs, resulting in a closed form of the ligand-binding domain. In full-length receptors, this domain closure is thought to lead to the opening of the ion channel (receptor activation). It has been observed that different agonists and antagonists can induce a range of domain movements, from domain opening of ca. 5°

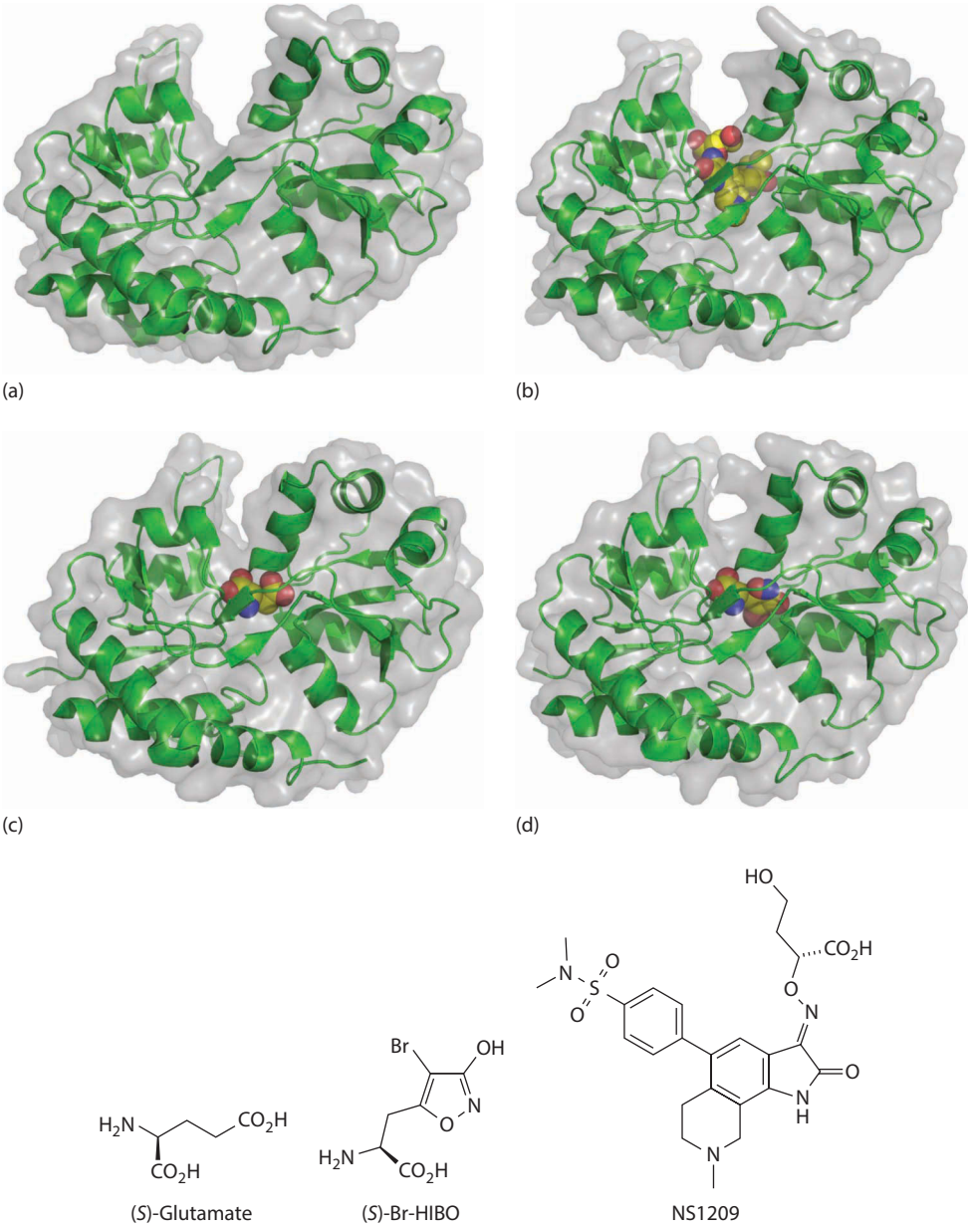

FIGURE 4.12 Structures of the soluble ligand-binding domain of the ionotropic glutamate receptor GluA2. (a) The open, unbound form of GluA2 (pdb-code 1FTO). (b) The NeuroSearch compound NS1209 stabilizes GluA2 in the open form (pdb-code 2CMO). (c) The endogenous ligand (*S*)-glutamate introduces domain closure of GluA2 by a "Venus flytrap" mechanism (pdb-code 1FTJ). (d) Various synthetic agonists (here (*S*)-Br-HIBO) also introduce domain closure in GluA2 (pdb-code 1M5C). Below: chemical structures of (*S*)-glutamate, the agonist (*S*)-Br-HIBO, and the antagonist NS1209.