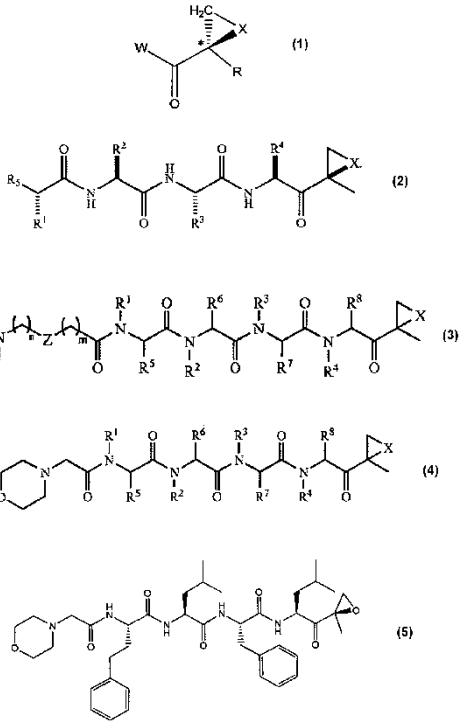
Cyclodextrin Complexation Methods for Formulating Peptide Proteasome Inhibitors

Abstract

This disclosure provides methods for formulating compositions comprising one or more peptide proteasome inhibitors and a cyclodextrin, particularly a substituted cyclodextrin. As well as cyclodextrin complexation methods of formulating a peptide proteasome inhibitor (e.g., a compound of formula (1) - (5) or a pharmaceutically acceptable salt thereof) with one or more cyclodextrins. Such methods substantially increase the solubility and stability of these proteasome inhibitors and facilitate both their manufacture and administration. For example, homogenous solutions of a compound of formula (5) (carfilzomib) can be obtained at a pharmaceutically useful pH (e.g., about 3.5) and at higher concentrations (e.g., about 5 mg/mL) than could be obtained without one or more cyclodextrins and the processes of complexation between the compound and one or more cyclodextrins provided herein.



[FIG. 1]