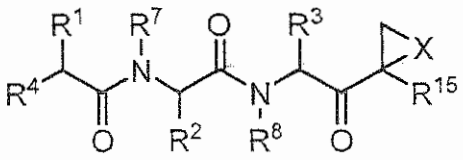
which replace their normal counterparts, β5, β1 and β2, respectively. When all three IFN-γ-inducible subunits are present, the proteasome is referred to as an "immunoproteasome". Thus, eukaryotic cells can possess two forms of proteasomes in varying ratios.

Through the use of different peptide substrates, three major proteolytic activities have been defined for the eukaryote 20S proteasomes: chymotrypsin-like activity (CT-L), which cleaves after large hydrophobic residues; trypsin-like activity (T-L), which cleaves after basic residues; and peptidylglutamyl peptide hydrolyzing activity (PGPH), which cleaves after acidic residues. Two additional less characterized activities have also been ascribed to the proteasome: BrAAP activity, which cleaves after branched-chain amino acids; and SNAAP activity, which cleaves after small neutral amino acids. Although both forms of the proteasome possess all five enzymatic activities, differences in the extent of the activities between the forms have been described based on specific substrates. For both forms of the proteasome, the major proteasome proteolytic activities appear to be contributed by different catalytic sites within the 20S core.

There are several examples of small molecules which have been used to inhibit proteasome activity; however, these compounds generally lack the specificity to delineate between the two forms of the proteasome. What is needed are improved compositions and methods for preparing and formulating proteasome inhibitor(s).

Summary ~~of the Invention~~

One embodiment~~aspect~~ of the disclosure~~invention~~ relates to crystalline compounds having a structure of Formula (I) or a pharmaceutically acceptable salt thereof,



(I)

wherein

each Ar is independently an aromatic group optionally substituted with 1 to 4 substituents;

each A is independently selected from C=O, C=S, and SO_2; or

R^{11} and R^{12} are independently selected from hydrogen, metal cation, C_{1-6}alkyl, C_{1-6}alkenyl, C_{1-6}alkynyl, aryl, and C_{1-6}aralkyl;

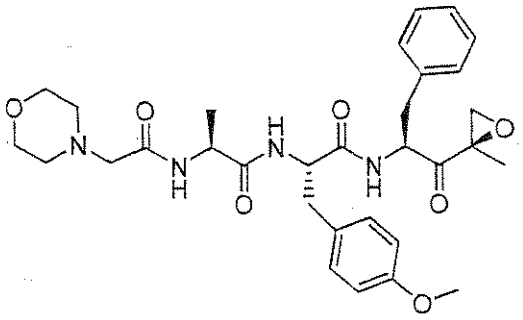
each R^{13} is independently selected from hydrogen and C_{1-6}alkyl; and

R^{14} is independently selected from hydrogen, C_{1-6}alkyl, C_{1-6}alkenyl, C_{1-6}alkynyl, carbocyclyl, heterocyclyl, aryl, and C_{1-6}aralkyl;

R^{15} is selected from C_{1-6}alkyl, C_{1-6}hydroxyalkyl, C_{1-6}alkoxy, -C(O)OC_{1-6}alkyl, -C(O)NHC_{1-6}alkyl, and C_{1-6}aralkyl;

provided that in any occurrence of the sequence ZAZ, at least one member of the sequence must be other than a covalent bond.

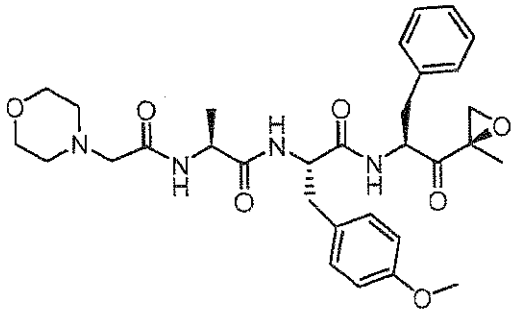
In one aspect, there is provided a crystalline compound having a structure of Formula (II)



(II)

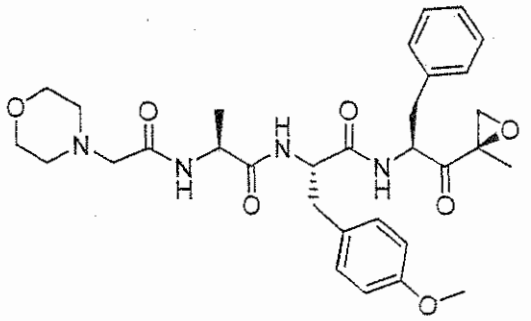
wherein the crystalline compound has 2θ values 3.62±0.20; 6.52±0.20; 7.20±0.20; 8.66±0.20; 10.04±0.20; 10.82±0.20; 12.98±0.20; 14.42±0.20; 16.46±0.20; 17.32±0.20; 17.98±0.20; 18.02±0.20; 18.88±0.20; 19.06±0.20; 19.56±0.20; 19.88±0.20; 20.40±0.20; 21.36±0.20; 22.16±0.20; 23.20±0.20; 25.40±0.20; and 28.82±0.20.

Another embodiment~~aspect~~ of the disclosure~~invention~~ relates to a crystalline compound of Formula (II)



(II)

In one aspect, there is provided a method for preparing a crystalline compound of Formula (II)



(II)

wherein the crystalline compound has 2θ values 3.62±0.20; 6.52±0.20; 7.20±0.20; 8.66±0.20; 10.04±0.20; 10.82±0.20; 12.98±0.20; 14.42±0.20; 16.46±0.20; 17.32±0.20; 17.98±0.20; 18.02±0.20; 18.88±0.20; 19.06±0.20; 19.56±0.20; 19.88±0.20; 20.40±0.20; 21.36±0.20; 22.16±0.20; 23.20±0.20; 25.40±0.20; and 28.82±0.20,

comprising (i) preparing a solution of a compound of Formula (II) in an organic solvent;

(ii) bringing the solution to supersaturation to cause formation of crystals; and

(iii) isolating the crystals.

In one aspect, there is provided the use of a crystalline compound as defined herein in the manufacture of a medicament for treating a disease or condition selected from an immune-related disease, cancer, inflammation, infection, proliferative disease, or neurodegenerative disease.

Brief Description of the Figures

Figure 1 shows a DSC thermogram of the crystalline toluene solvate of Compound 1.

Figure 2 shows an XRPD of the crystalline toluene solvate of Compound 1.

Figure 3 shows a TG thermogram of crystalline toluene solvate of Compound 1.

Figure 4 shows an ORTEP diagram of a single molecule of the of crystalline toluene solvate of Compound 1.

Figure 5 shows a DSC thermogram of an amorphous form of Compound 1.

Figure 6 shows an XRPD pattern of an amorphous form of Compound 1.