including but not limited to, a metal-based impurity.

[0019a] In one aspect, there is provided a process for preparing 5-azacytidine, or a solvate, hydrate, or polymorph thereof, comprising the steps of reacting a silylated 5-azacytosine with a protected β-D-ribofuranose in the presence of a metallic Lewis acid to yield a protected 5-azacytidine, deprotecting the protected 5-azacytidine to yield 5-azacytidine, contacting the 5-azacytidine with an acid to yield a salt of 5-azacytidine, contacting the salt of 5-azacytidine with a base to yield 5-azacytidine, and re-crystallizing the 5-azacytidine to yield 5-azacytidine, or a solvate, hydrate, or polymorph thereof, that is free of metal-based impurities.

[0020] In one embodiment, provided herein is a salt of 5-azacytidine, including, but not limited to, hydrochloric acid salt, sulfuric acid salt, hydrobromic acid salt, and methanesulfonic acid salt. In one embodiment, provided herein is 5-azacytidine hydrochloric acid salt. In one embodiment, provided herein is a salt of 5-azacytidine that is substantially free of one or more impurities, such as for example, a metal-based impurity. In one embodiment, provided herein is a pharmaceutically acceptable salt of 5-azacytidine, including, but not limited to hydrochloric acid salt, sulfuric acid salt, hydrobromic acid salt, and methanesulfonic acid salt. In one embodiment, provided herein is a pharmaceutically acceptable salt of 5-azacytidine that is substantially free of one or more impurities, such as for example, a metal-based impurity.

[0021] In specific embodiments, provided herein are processes for preparing 5-azacytidine, or a salt, solvate, hydrate, or polymorph thereof, comprising any one, two, three, four, five, or six of the steps of:

(a) reacting 5-azacytosine with a silylating reagent to yield a silylated 5-azacytosine;

(b) reacting the silylated 5-azacytosine with an acyl protected β-D-ribofuranose in the presence of a metallic Lewis acid; and quenching the reaction with water and at least one neutralizing reagent to yield a protected 5-azacytidine;

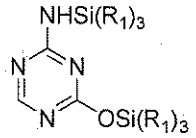
(c) reacting the protected 5-azacytidine with a base, selected from the group consisting of alkoxide, ammonia, and tetra-substituted ammonium hydroxide, in an alcohol to yield 5-azacytidine;

(d) contacting the 5-azacytidine from step (c) with an acid in an organic solvent to yield a salt of 5-azacytidine;

(e) contacting the salt of 5-azacytidine from step (d) with a base in an organic solvent to yield 5-azacytidine as a free base; and

(f) re-crystallizing the 5-azacytidine from step (e).

[0022] In one embodiment, the silylated 5-azacytosine is a compound of formula (A):



(A),

wherein each R_1 is independently optionally substituted C_1–C_{10} alkyl, optionally substituted C_3–C_{10} cycloalkyl, or optionally substituted C_6–C_{10} aryl. In some embodiments, R_1 is straight chain alkyl, branched alkyl, cycloalkyl, or aryl, including but