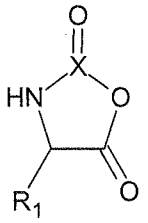
cyclocondensation shown often requires high temperatures or harsh conditions to achieve full cyclization. Further, it is not compatible with each N-protecting group that might be necessary for further derivatization of the exo-cyclic nitrogens.

[0013] Some useful N-protecting groups include acetyl, trichloroacetyl, trifluoroacteyl and other amide forming protecting groups; carbamate protecting groups including benzyloxycarbonyl (Cbz) and t-butoxycarbonyl (BOC) among others.

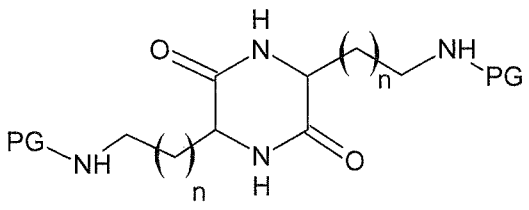
[0014] In an embodiment, a method for the synthesis of a 3,6-aminoalkyl-2,5-diketopiperazine is provided. The method comprises, adding a cyclic α-N protected active amino ester according to the formula below:



wherein R_1 is a N-protected amino C_1 to C_8 alkyl, and X is C, S or P, to a mixture of an amine catalyst in an organic solvent.

[0015] In an embodiment, a method for the synthesis of a 3,6-aminoalkyl-2,5-diketopiperazine is provided. The method comprises, adding a cyclic α-N protected active amino ester to a mixture of an amine catalyst in an organic solvent. In certain embodiments, the method provides 3,6-aminoalkyl-2,5-diketopiperazine in a yield of greater than 40 % (i.e., 40 to 100 %).

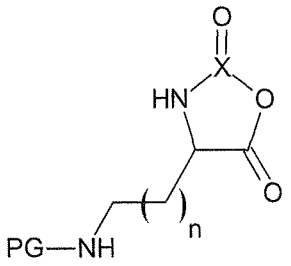
[0015a] In an embodiment, there is provided a method for the synthesis of a N-protected bis-3,6-aminoalkyl-2,5- diketopiperazine of Formula I,



Formula I

wherein PG is selected from CBz, Boc, trifluoroacetyl, and acetyl and wherein n is from 1 to 8;

the method comprising: adding a cyclic α-N protected active amino ester according Formula II



Formula II

wherein PG is selected from CBz, Boc, trifluoroacetyl, and acetyl, wherein X is selected from C, S, and P, and wherein n is from 1 to 8; to a mixture of an amine catalyst in an organic solvent, the amine catalyst selected from the group comprising: aziridine and benzamidoxime.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] Figure 1 is a reaction scheme showing an exemplary embodiment of a route for the formation of 3,6-aminoalkyl-2,5-diketopiperazine through a cyclic N-carboxy anhydride (NCA) intermediate.

[0017] Figure 2 is a bar graph showing results for a survey of several organic solvents.