

Formation of N-Protected bis-3,6(4-aminoalkyl)-2,5-diketopiperazineABSTRACT

The disclosed embodiments detail improved methods for the synthesis of diketopiperazines from amino acids. In particular improved methods for the cyclocondensation and purification of N-protected 3,6-(aminoalkyl)-2,5-diketopiperazines from N-protected amino acids. Disclosed embodiments describe methods for the synthesis of 3,6-bis-[N-protected aminoalkyl]-2,5-diketopiperazine comprising heating a mixture of an amino acid in the presence of a catalyst in an organic solvent. The catalyst is selected from the group comprising sulfuric acid, phosphoric acid, p-toluenesulfonic acid, 1 - propylphosphonic acid cyclic anhydride, tributyl phosphate, phenyl phosphonic acid and phosphorous pentoxide among others. The solvent is selected from the group comprising: dimethylacetamide, N-methyl-2-pyrrolidone, diglyme, ethyl glyme, proglyme, ethyldiglyme, m-cresol, p-cresol, o-cresol, xylenes, ethylene glycol and phenol among others.

Figure 1