

SYNLETT Spotlight 220

1,1'-Carbonyldiimidazole (CDI)

Compiled by Rohit K. Sharma



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Rohit K. Sharma was born in Chandigarh, India in 1980. He obtained his B.Sc. (Honors) in chemistry in 2002 and M.Sc. (Honors) in chemistry in 2004 from Panjab University. After that, he joined the research group of Dr. Rahul Jain at the National Institute of Pharmaceutical Education & Research (NIPER) in 2004 and is currently working towards his Ph.D. His main interests lie in the development of synthetic methodologies, biological evaluation and mechanistic studies of antimicrobial peptides, peptoids, and unnatural amino acids.

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Introduction

1,1'-Carbonyldiimidazole (CDI; Figure 1, **1**), a white crystalline solid with its melting point between 117 °C and 122 °C, has been widely exploited in organic chemistry for carrying out reactions involving transfer of a carbonyl group,^{1–3} imidazole moiety,⁴ and coupling between different functional groups under various conditions.^{5–9}

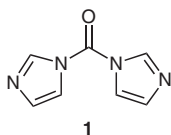
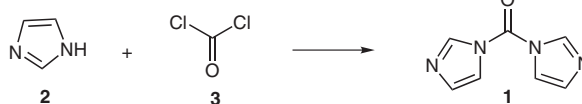


Figure 1

Preparation

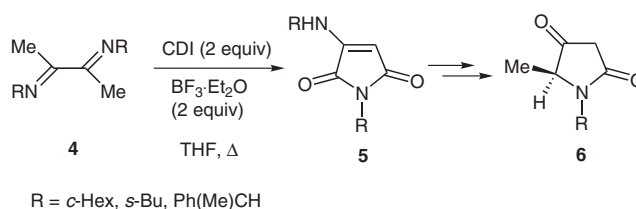
1,1'-Carbonyldiimidazole (CDI, **1**) can be readily prepared by the reaction of four equivalents of imidazole **2** with phosgene (**3**) under anhydrous conditions (Scheme 1). The imidazole serves as both nucleophile and base in this conversion. Removal of the side product, imidazolium chloride, and solvent results in the crystalline product in ca. 90% yield.



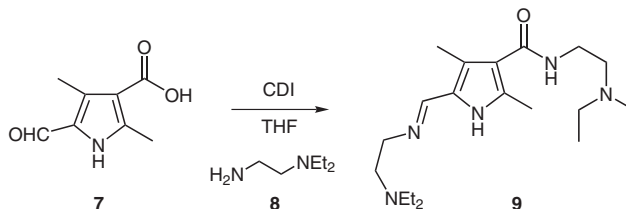
Scheme 1

Abstracts

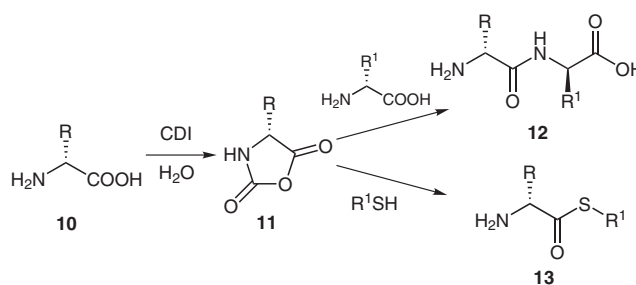
(A) 1,1'-Carbonyldiimidazole (CDI) has been efficiently employed in asymmetric synthesis of tetramic acid derivatives **6**. In this reaction, CDI transfers a carbonyl group to α -diimines **4** in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ to afford *N*-alkyl-4-alkylamino-5-methylene-pyrrol-2-ones **5** in moderate yields. The total asymmetric synthesis of tetramic acid derivatives **6** involves four steps in which the key step is a carbonyl transfer from CDI to the α -ketodiimine.¹



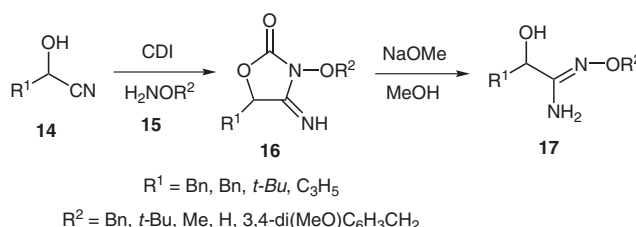
(B) Amidation reactions between different sterically hindered acid aldehydes and amines have been reported to be efficiently catalyzed by CDI. First, compound **7** is activated with CDI, then, addition of *N,N*-diethylethylenediamine (**8**) to the reaction mixture leads to the imine amide product **9**. Remarkable rate enhancement was observed in the reaction due to catalysis by the released carbon dioxide.⁵



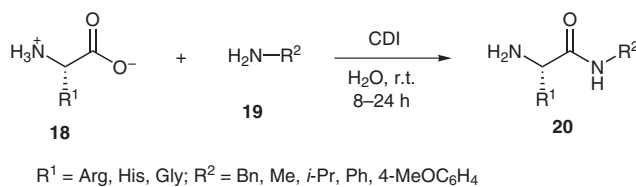
(C) The aqueous CDI-based synthetic method offers an easy and inexpensive way to prepare peptides and peptide thioesters. The synthesis involves reaction of amino acid **10** with CDI to give the amino acid carboxyanhydride intermediate **11** that condenses to both dipeptide **12** and dipeptide thioester **13** in the presence of added amino acid or thiol. Repeated aminoacylation steps on these dipeptide derivatives produce peptide and peptide thioester chains.^{6–8}



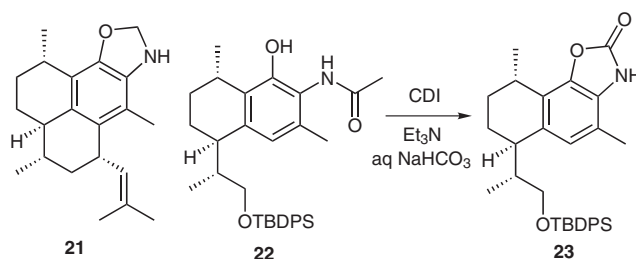
(D) Cyanohydrins **14** on stepwise reaction with CDI and O-substituted hydroxylamines **15** give O-substituted 3-hydroxy-4-iminoxazolidin-2-ones **16** in a high-yielding one-pot synthesis.² Then, sodium methoxide mediated conversion of **16** produces the corresponding O-substituted α -hydroxyamidoximes **17**.



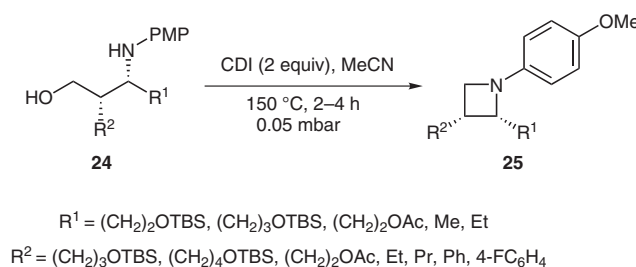
(E) Recently, the first amidation reaction of unprotected α -amino acids in water under neutral conditions with various aliphatic, aromatic, and heteroaromatic primary amines in the presence of CDI at ambient temperature was reported.⁴ Zwitterionic amino acids **18** first react with CDI leading to the formation of the intermediate mixed anhydride, followed by nucleophilic attack of amines **19** facilitating the formation of amides **20** in moderate yields.



(F) In one of the steps in an enantiospecific pathway described by Davidson and Corey to synthesize an antitubercular tetracyclic oxazole marine natural product called pseudopteroxazole **21**, cyclization of the phenol derivative **22** with CDI gave the cyclic carbamate **23** in 94% yield.³



(G) Cyclization of various γ -amino alcohols **24** to substituted azetidines **25** and other N-heterocycles has been conveniently carried out in quantitative yields by using 1,1'-carbonyldiimidazole.⁹ CDI efficiently activates the hydroxyl groups avoiding the use of toxic reagents and tolerating a wide variety of functional groups.



References

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