

SYNLETT Spotlight 304

1-Ethyl-3-(3-dimethylaminopropyl) Carbodiimide Hydrochloride (EDCI·HCl)



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

Compiled by Navneet Goyal

Navneet Goyal was born in Dhand, Haryana, India in 1982. After obtaining his B.Sc. (Honors) in Chemistry in 2002 and M.Sc. (Honors) in Chemistry in 2004 from Panjab University, Chandigarh, India, he worked for two years at Aurigene Discovery Technology, a pharmaceutical company at Bangalore, India. In 2006, he joined the research group of Prof. Guijun Wang at the University of New Orleans, and now he is working towards his Ph.D. His research interest mainly lies on synthesis and biological evaluation of carbohydrate- and peptide-based small molecules.

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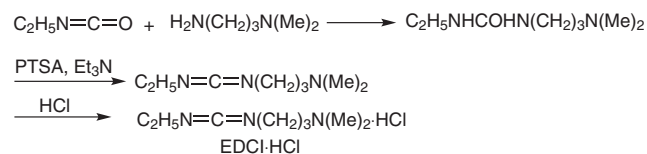
Dedicated to my research advisor Prof. Guijun Wang

Introduction

1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDCI·HCl)¹ is a white crystalline solid with a melting point of 110–115 °C. EDCI·HCl is a versatile organic reagent for many reactions. It is an effective dehydrating agent commonly used in the synthesis of amides, esters and anhydrides.² In these reactions, an acyl urea is a byproduct, which is water-soluble. This property of EDCI·HCl makes it a very important chemical in its own class, superior to other traditional coupling reagents. It can also be used in the synthesis of oxazoles, oxadiazoles, triazoles, and guanidine compounds.

Preparation of EDCI·HCl:

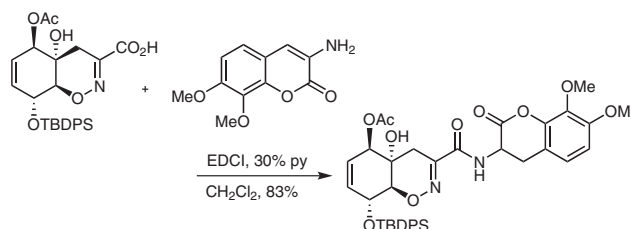
EDCI·HCl is commercially available. It can be prepared (Scheme 1) by coupling ethyl isocyanate with *N,N*-dimethylpropane-1,3-diamine to give a urea, followed by dehydration and treatment with HCl.³



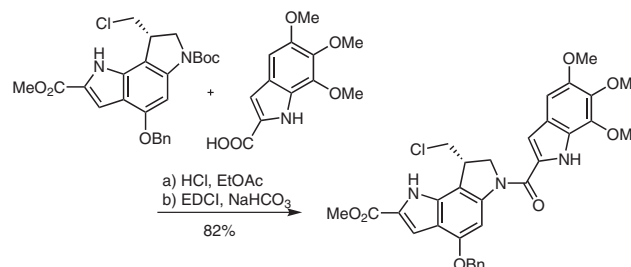
Scheme 1

Abstracts

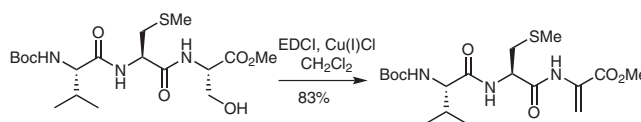
(A) Conjugation of acids with aromatic amines generally leads to poor yields of amides. However, when performed with EDCI·HCl, coupling between an acid and an amine with low nucleophilicity yields 83% of the product.⁴



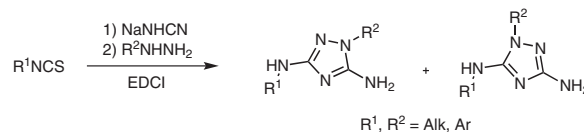
(B) In the penultimate step of the total synthesis of *iso*-duocarmycin SA, direct coupling of the secondary amine with the corresponding acid using EDCI·HCl afforded 82% of the product in 30 minutes without any racemization.⁵



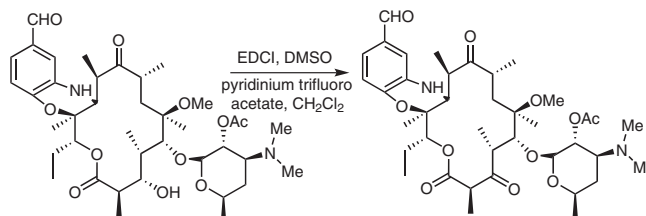
(C) EDCI-HCl can be used for dehydration of an alcohol. Chapman et al. dehydrated the serine residue using EDCI-HCl and CuCl to provide the dehydroalanine-containing peptide Boc-Val-Cys-Ala-OMe.⁶



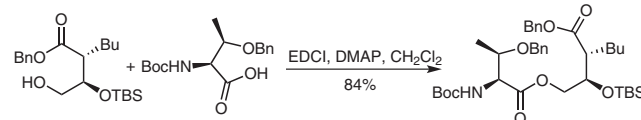
(D) 1,2,4-Triazole-3,5-diamine derivatives were synthesized in moderate to high yields in a one-pot reaction from the corresponding isothiocyanates, mono-substituted hydrazines, and sodium hydrocyanamide, in the presence of EDCI-HCl.⁷



(E) Selective oxidation of an alcohol into a ketone can be performed using EDCI-HCl and DMSO under Pfitzner-Moffatt oxidation reaction conditions.⁸



(F) Esters can be formed using EDCI-HCl. In the synthesis of novel analogues of antimycin A₃ EDCI-HCl was used to synthesize an important intermediate ester.⁹



References

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