Water Soluble Carbodiimide

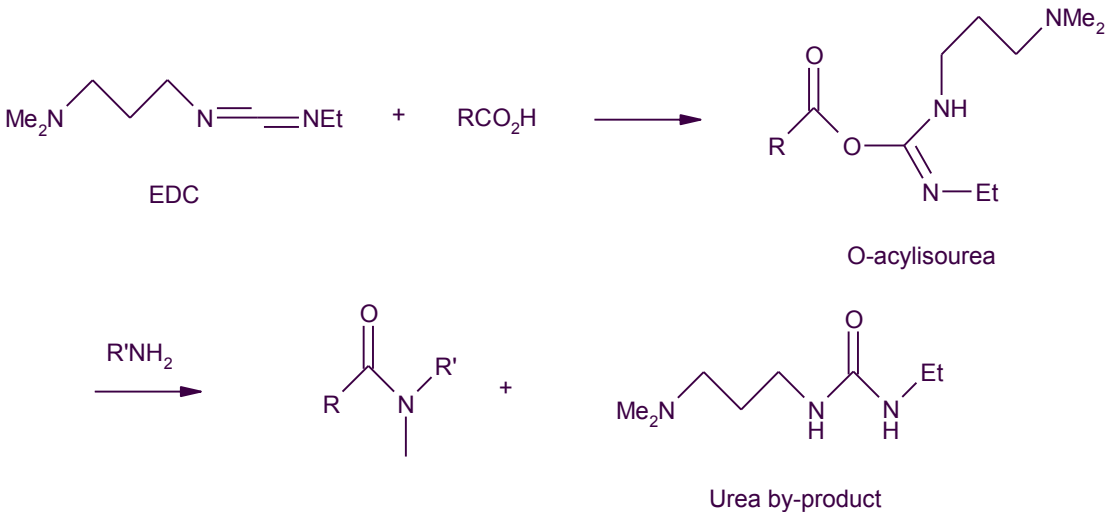
Product Code: **FD05800**
CAS Number: **25952-53-8**
Chemical Formula: **$C_8H_{17}N_3.HCl$**
Molecular Weight: **134.13**

Synonyms: *1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide HCl*
EDC
WSC
EDAC

1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, usually known as water soluble carbodiimide, EDC, EDAC or WSC is a versatile modern coupling agent for the synthesis of pharmaceuticals. It is an easily handled solid which is now replacing (and is often superior to) N,N'-dicyclohexylcarbodiimide (DCC). EDC has a high solubility in water (> than 200g/l) and is also soluble in a variety of organic solvents e.g. dichloromethane, tetrahydrofuran and dimethylformamide.

Although EDC can be used for reactions in aqueous solution it is usually stored under dry conditions to prevent slow hydrolysis to the corresponding urea. EDC is not a strong skin sensitiser like DCC, but it is an irritant solid and should be handled with care.

The main advantage of EDC over DCC in peptide synthesis is in the ease of handling of the reagent, the enhanced solubility of EDC and particularly the urea by-product formed during the reaction. The urea by-product is readily soluble in water and can easily be removed by extraction. The DCC by-product, dicyclohexylurea, has to be removed from the reaction by multiple filtrations. EDC can be used in a wide range of solvents and under mild conditions. The most common reaction conditions involve using a solvent such as water, dichloromethane, tetrahydrofuran or dimethylformamide at room temperature for 6-12 hrs. The coupling of an acid to an amine to form a peptide bond in the presence of EDC proceeds via an O-acylisourea intermediate. The first step is rapid and the reaction of the O-acylisourea with the amine to form the peptide bond is a slower step as shown in Scheme 1.[1]



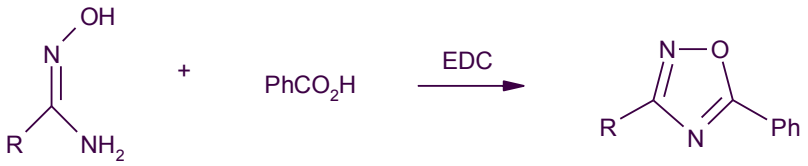
Scheme 1

Carbosynth Limited
8&9 Old Station Business Park - Compton - Berkshire - RG20 6NE - UK
www.carbosynth.com sales@carbosynth.com Tel: +44 1635 578444 Fax: +44 1635 579444

EDC is increasingly being used as a coupling agent in the preparation of new pharmaceutical substances. This is because of the ease of purification of the 'late stage' intermediate or active ingredient from the water soluble by-products.[2,3]

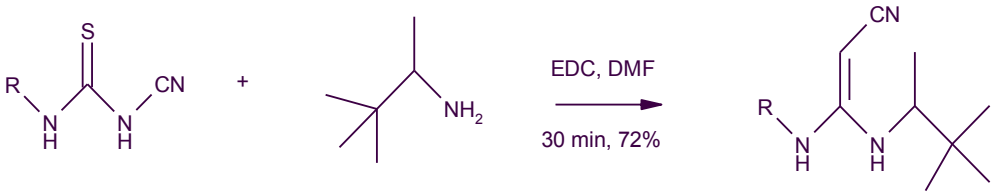
As well as being used for the synthesis of amides EDC is also used as a coupling agent in the preparation of esters from carboxylic acids using dimethylaminopyridine as catalyst. This procedure has been used to prepare *tert*-butyl esters of N-protected amino acids.[4]

The oxadiazole ring system (which is present in a range of pharmaceutical active products) has been synthesised using EDC to couple a carboxylic acid group to form the ring. This procedure has the advantage over other methods in that carboxylic acids are readily available and this procedure is compatible with a variety of functional groups (Scheme 2).[5]



Scheme 2

The cyanoguanidine group is also an important part of pharmaceutical products. The synthesis of cyanoguanidines from thioureas is greatly improved by the use of EDC as coupling agent compared with earlier methods using DCC. This is due to an easier work up and also the reaction proceeds faster and gives high yields at room temperature as shown in scheme 3.[6]



Scheme 3

EDC has also found wide use outside the area of pharmaceutical synthesis in the coupling biologically active molecules to supports. This has been applied to the area of combinatorial chemistry to attach carboxylic acids to a poly amine support. EDC has also been used in the preparation of bio-sensors e.g. the immobilization of DNA onto an EDC activated glassy carbon electrode to develop sequence selective detectors.[7]

EDC has also been used in developing hardeners for photographic films by activating carboxyl groups and thus aiding cross-linking. It has also been used as a polymerization activator for cross-linking on the surfaces of animal products for use in prosthetic implants.

References

1. J. C. Sheehan, J. Preston and P. A. Cruickshank; *J. Am. Chem. Soc.*, 1965, **87**, 2492.
2. J. A. Robl, C-Q. Sun, *et al*, *J. Med. Chem.*, 1997, **40**, 1570.
3. D. Hajiwara, H. Miyake, N. Igari, M. Karino, Y. Maeda, T. Fujii and M. Matsuo, *J. Med. Chem.*, 1994, **37**, 2090.
4. M. K. Dhaon, R. K. Olsen and K. Ramasamy, *J. Org. Chem.*, 1982, **47**, 1962.
5. G-B. Ling and D. D. Feng, *Tetrahedron Letters*, 1996, **37**, 6627.
6. K. S. Atwal, S. Z. Ahmed and B. C. O'Reilly, *Tetrahedron Letters*, 1989, **30**, 7313.
7. K. M. Millan and S. R. Mikkelsen, *Anal. Chem.*, 1993, **65**, 2317.