# *N,N'*-Disuccinimidyl carbonate (DSC)

***N,N'*-Disuccinimidyl carbonate (DSC)** is a crystalline reagent employed as a carbonyl equivalent. DSC is stable at room temperature, only slightly sensitive to humidity. Its physical and toxicological properties make it a convenient, easy-to-handle reagent. However, difficulties in manufacturing DSC on reasonable scale have limited its use to the lab.

*Ubichem recently developed and scaled-up a commercial process to make DSC at our facilities in Budapest, Hungary. The compound was required for the synthesis of an API entering clinical development, and is now available for general sale. The product can be manufactured in ton scale if required.*

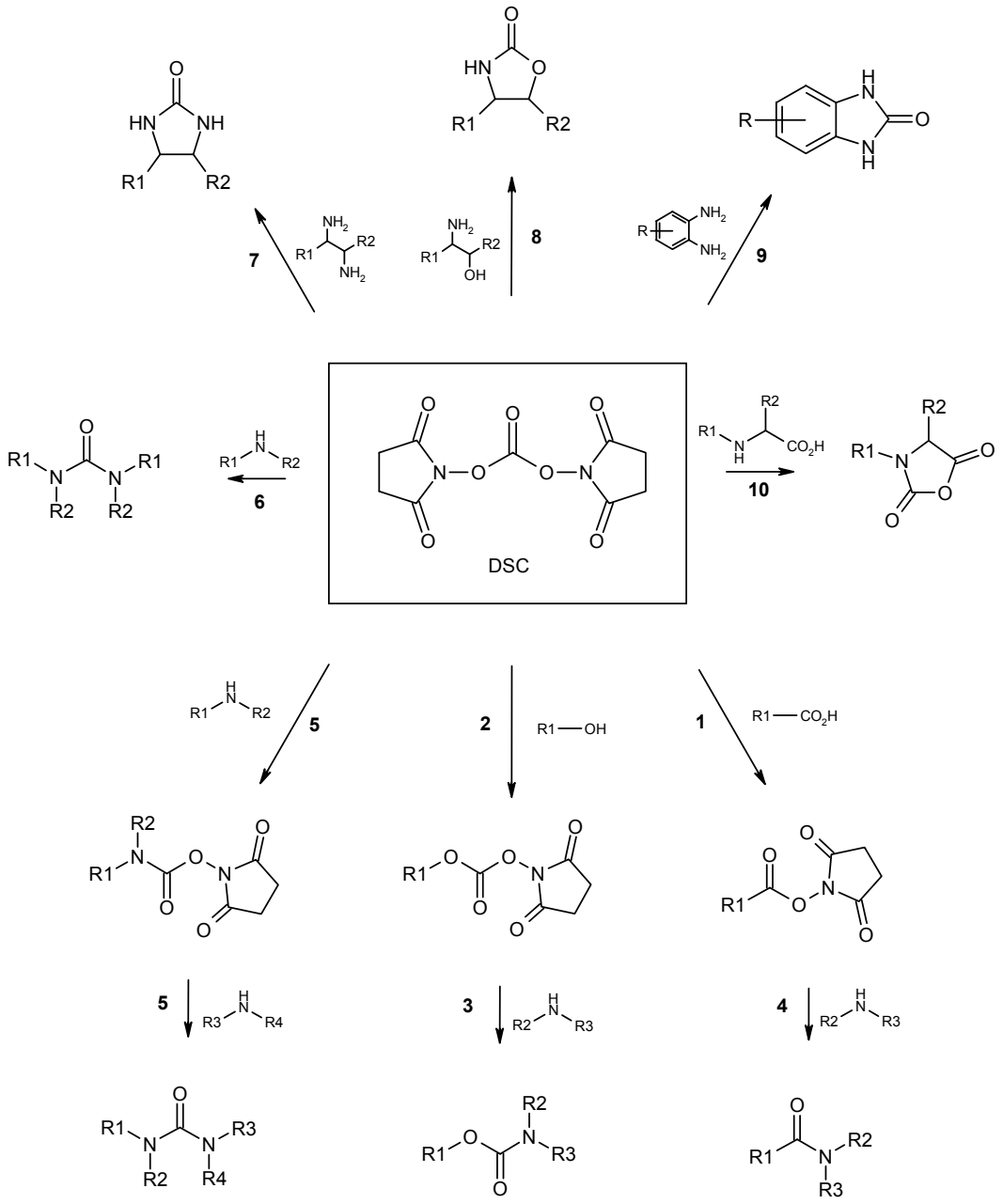


Figure 1. DSC applications

***Preparation of active esters and mixed carbonates (path 1 and 2, Figure 1)*:**
DSC is well known as an activating agent in peptide chemistry[1,2].It reacts with the carboxylic group of an acylamino acid to yield the N-succinimidyl (OSu) ester: an active ester[1]. Numerous examples can be found in the literature (with or without isolation) as intermediates for preparation of amides and carbamates (see below). Amongst these, some very specific examples can be found: eg DSC is used for the efficient preparation of an active carbonate hydroxypolystyrene resin in biologically active peptide synthesis (alcohol, carbamate and cyclic peptide)[3,4].

***Preparation of carbamates (path 3, Figure 1):***
Reaction of DSC with alcohols followed by addition of primary or secondary amines forms a carbamate at room temperature in high yield[5-7].
On the other hand, DSC reacts with an amine give an active carbamate molecule[8-10]. This type of compound is a suitable reagent for further transformation, for example urea synthesis (see mixed ureas).

***Preparation of amides (path 4, Figure 1):***
Active esters formed from DSC and a carboxylic acid can be cleaved with an amine resulting in a carboxamide group. Due to the mild reaction conditions, this reaction is widely used in many fields of synthetic organic chemistry especially in amino acid and peptide chemistry[11-15].

***Preparation of ureas (path 5 and 6, Figure 1):***
DSC - as a carbonyl equivalent - is a suitable precursor to various substituted urea derivatives. Reaction of DSC with an excess of primary or secondary amine results in symmetrical ureas. On treatment with equimolar amount of amine, an active carbamate imtermediate can be obtained. This carbamate may react with an other amine molecule to give a mixed urea in good yield[8].

***Carbonyl insertion reactions (path 7-9, Figure 1):***
DSC is a useful cyclizing reagent in heterocyclic chemistry. It reacts with 1,2-disubstituted aromatic and aliphatic compounds, forming various heterocyclic systems: 1,2-diamines,
1,2-aminoalcohols and 1,2-aminothiols give imidazolones, oxazolones and thiazolones and their fused derivatives, respectively[16-17]. □,□-Amino acids can be transformed into large membered lactam rings[18]. These transformations can be performed in liquid phase and solid phase, as well. Some solid phase synthsis of heterocyclic ring systems is described in the literature[19-20].

***Preparation of amino acid N-carboxy anhydrides (path 10, Figure 1)[21]:***
The standard procedure for preparing N-carboxy anhydrides (NCAs) of amino acids is by means of phosgene (although Ubichem uses triphosgene). In addition to requiring special safety precautions, this reaction proceeds with the formation of two equivalents of HCl. Undesired side reactions - caused by HCl - can be avoided using DSC as cyclising agent. The neutral and mild reaction conditions allow safe preparation of new acid-labile derivatives for peptide synthesis.

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