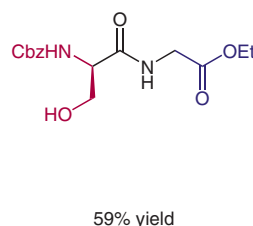
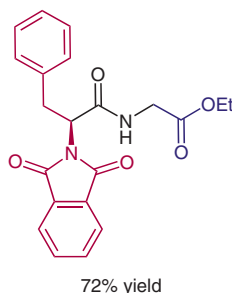
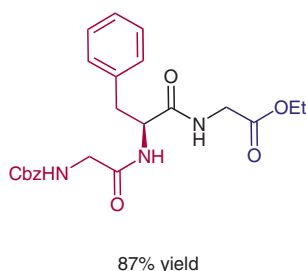
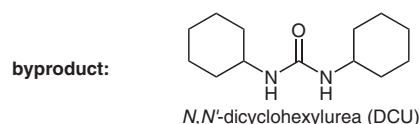
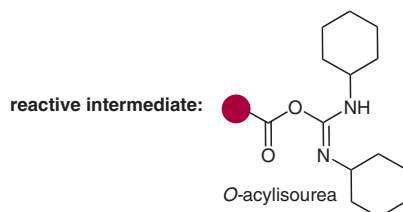
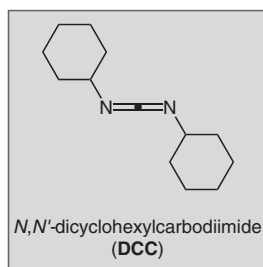
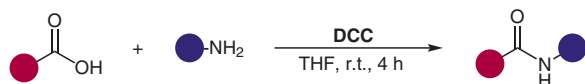


J. C. SHEEHAN, G. P. HESS (MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, USA)

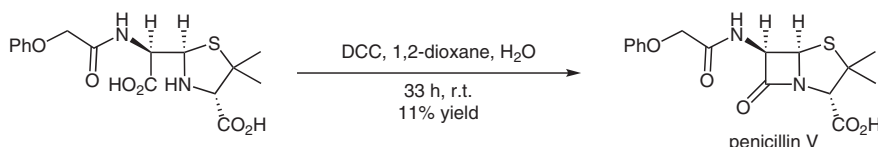
A New Method of Forming Peptide Bonds

*J. Am. Chem. Soc.* **1955**, *77*, 1067–1068.

## A Classic Way of Forming Amide Bonds



First application in natural product synthesis:



**Significance:** DCC is a versatile carbodiimide reagent that is used in oxidation or dehydration reactions. Sheehan and Hess reported the discovery of DCC for the synthesis of amides in 1955. In subsequent work, Sheehan and his co-worker describe how DCC enabled the total synthesis of penicillin V by formation of the central  $\beta$ -lactam ring (*J. Am. Chem. Soc.* **1957**, *79*, 1262). Carbodiimide reagents are still among the most widely used coupling reagents in academia and industry.

**Comment:** DCC activates carboxylic acids to the *O*-acylisourea, which can then react with amines to form an amide bond. The reaction proceeds fast, is high-yielding and tolerates water, and the polar side product DCU can be removed by precipitation. However, DCC is a potent skin sensitizer and should be handled with caution. Modern coupling reagents are water-soluble and decrease racemization rates.

Category

Chemistry in  
Medicine and  
Biology

Key words

coupling reagents

DCC

amide bonds

penicillin V

Synfact  
Classic

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