Tetrahedron Letters,Vol.22,No.48,pp 4817-4818,1981 0040-4039/81/484817-02$02.00/0
Printed in Great Britain

β-ELIMINATION OF β-HYDROXYAMINO ACIDS WITH DISUCCINIMIDO CARBONATE

Haruo Ogura,* Osamu Sato, and Kazuyoshi Takeda

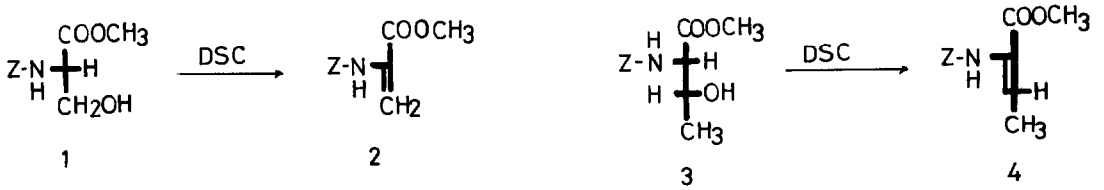
School of Pharmaceutical Sciences, Kitasato University

Shirokane, Minato-ku, Tokyo 108, Japan

Summary: Direct eliminations of β-hydroxyl groups and active ester formations from β-hydroxy amino acids under a one-step reaction with disuccinimido carbonate (DSC) are reported.

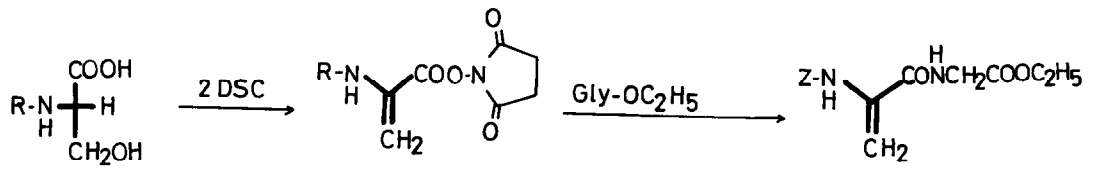
α,β-Unsaturated α-amino acids are of great importance as starting materials for the syntheses of dehydropeptide and peptide antibiotics.[1-4] Conversions of threonine derivatives to dehydroamino acids by the eliminations of β-chloro and o-tosyl radicals have been reported by Srinivasan et al.[5]

In this paper, we report on direct eliminations of hydroxyl groups and active ester formations from β-hydroxy α-amino acids under a one-step reaction. Recently, we synthesized disuccinimido carbonate (DSC)[6] for the purpose of using it as a reagent for active ester syntheses. DSC was applied to Z-glutamine and Z-serine and a small amount of respective dehydroxy product was obtained.[7] This finding will lead to a new method of preparing dehydroamino acids.

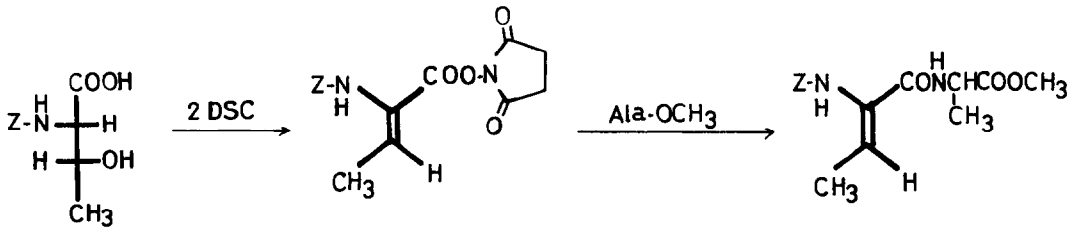


1 2 3 4

Treatment of methyl ester of Z-serine (1) with equimolar DSC and triethylamine in acetonitrile caused β-elimination of the hydroxyl group after the mixture had been left for 4 hr at room temperature, and Z-ΔAla-OMe (2) was obtained in 90% yield. A similar treatment of methyl ester of Z-threonine (3) with DSC yielded Z-ΔBut-OMe (4) mp 65-66° (reported[5] mp 65.5-67°) in 70% yield after recrystallization from benzene-pet. ether. It was made clear from the NMR spectrum of the product that Z isomer was the only product and E isomer was not formed.



5a: R=Z, 5b: R=Boc 6a: R=Z, 6b: R=Boc 7



8 9 10

Similarly Z- (or Boc-)serine (5a,b) was treated with DSC in a 1:2 molar ratio and Z- or Boc-ΔAla-OSu (6a,b) was obtained quantitatively. Treatment of 6a with ethyl ester of glycine yielded Z-ΔAla-Gly-OEt (7) mp 78-79° in 82% yield.

When Z-threonine (8) was treated with DSC in a 1:2 molar ratio Z-ΔBut-OSu (9) was obtained quantitatively (mp 103-104°). Since the product from 3 and DSC was proved to be Z isomer as described above, this compound (9) is also considered to have Z configuration. Treatment of 9 with methyl ester of alanine yielded Z-ΔBut-Ala-OMe (10) in 86% yield.

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(Received in Japan 23 September 1981)