A Crystalline Active Ester of Benzyloxycarbonylserine

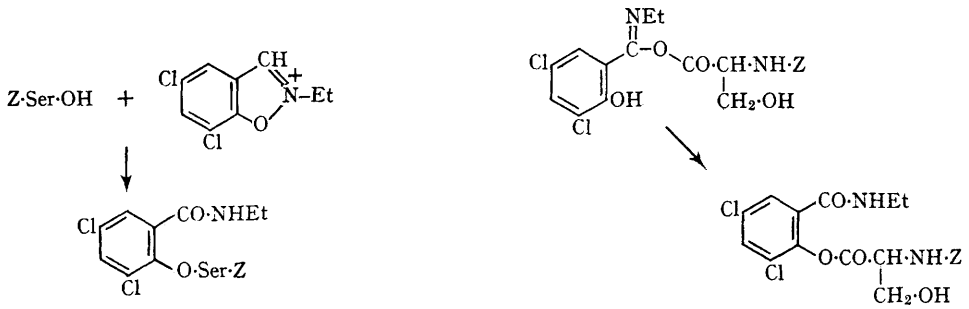
By S. RAJAPPA and A. S. AKERKAR
(*CIBA Research Centre, Goregaon, Bombay* 63)

IN the course of an investigation of the usefulness of the benzisoxazolium cation described by Woodward and Kemp,[1] we felt that introduction of electron-withdrawing substituents in the benzene ring might prove beneficial by increasing the "activity" of the intermediate active esters. Accordingly, commercially available 3,5-dichlorosalicylaldehyde was converted into 5,7-dichloro-*N*-ethyl benzisoxazolium fluoroborate by the procedure described by Kemp and Woodward.

We now find that the reagent reacts with a variety of *N*-protected amino-acids to give crystalline active esters in good yield. Even benzyloxycarbonylserine gives a crystalline active ester in 70—80% yield. Addition of the reagent as a solid to a cooled (ice–salt), stirred solution of benzyloxycarbonylserine and triethylamine in methylene chloride gave the active ester in a few minutes as a crystalline solid: m.p. 118—121° or 156—160° (dimorphous forms; identical i.r. spectra in solution) i.r. (Nujol): 3400, 3310, 3260 sh, 1780, 1690, and 1655 cm.$^{-1}$.

The product has been reacted with glycine *p*-nitrobenzyl ester to provide the protected dipeptide[2] in 78·5% yield.

The great difficulty in making active esters of benzyloxycarbonylserine has been commented upon recently by Bodanszky and Ondetti.[3] The



Z = benzyloxycarbonyl

success in the present instance evidently depends on the fact that the crucial reaction involves an intramolecular nucleophilic displacement by a phenol rather than an intermolecular one as in those cases involving use of dicyclohexylcarbodiimide (DCCI).

We are extremely grateful to Professor T. R. Govindachari for his interest and encouragement.

(*Received, October 7th*, 1966; *Com.* 756.)

[1] D. S. Kemp and R. B. Woodward, *Tetrahedron*, 1965, **21**, 3019.
[2] B. Iselin and R. Schwyzer, *Helv. Chim. Acta.*, 1962, **45**, 1499.
[3] M. Bodanszky and M. A. Ondetti, *Chem. and Ind.*, 1966, 26.