

A NEW ROUTE TO HETEROCYCLIC α -DEHYDRO α -AMINO ESTERS

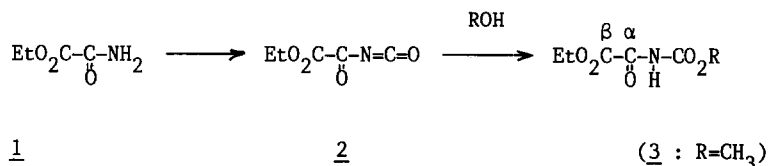
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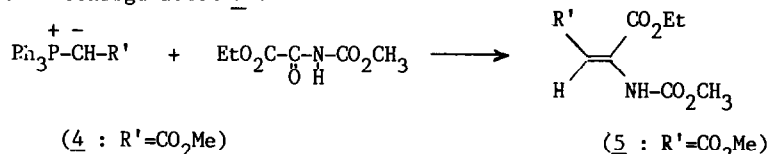
Abstract : Heterocyclic α -dehydro α -amino esters are obtained by the reaction of ethyl N-carbomethoxy oxamate with ω -halogened phosphorus ylids.

In the preceding paper (1), we reported a novel synthesis of α -dehydro α -amino esters by condensation of phosphorus ylids with t-butoxalyl iminoether. In this paper, we wish to describe a novel procedure for synthesizing heterocyclic α -dehydro α -amino esters from ethyl N-carbomethoxy oxamate 3.

Ethyl N-carboethoxy oxamate has been prepared from ethoxalyl chloride and ethyl carbamate (2) but the yield was rather low. We give herein a general procedure which may be adapted for the preparation of all ethyl N-carboalkoxy oxamates. This method is based on the use of the intermediate ethoxalyl isocyanate 2 (3) :

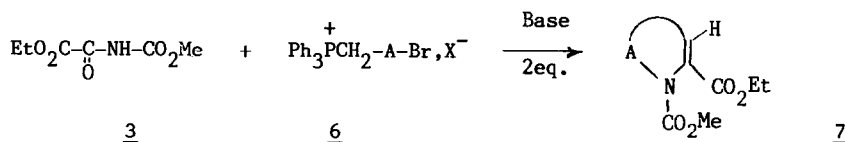


Compound 3 does not undergo attack at the β -position by phosphorus ylid 4 as oxamate does (4), but instead provides an attack at the α -position and leads to the α -dehydro amino ester of Z configuration 5 :



It is evident that basic ylids (R'=alkyl or phenyl) cannot be used because of the high acidity of the NH group. However we have found that oxamate 3 can be easily alkylated and used as precursor for heterocyclic α -dehydro α -amino esters.

Thus, compounds 7 were obtained by a one-step procedure from ω -halogenoalkyltriphenyl phosphonium salts (table).



$\text{Ph}_3\text{PCH}_2^+\text{---A-Br} \text{ Br}^- \underline{6}$	<u>7</u>	Yield (%)	mp or bp (°C) or (°C/mm)
A-Br			
<u>6a</u> COCH_2Br		60 ^a	66
<u>6b</u> $\text{CH}_2\text{CH}_2\text{Br}$		68 ^b	110/2.1
<u>6c</u> $\text{CH}_2\text{CH}_2\text{CH}_2\text{Br}$		40 ^c	130/1.3
<u>6d</u> $\text{o-C}_6\text{H}_4\text{CH}_2\text{Br}$		61 ^b	135/1.3

(a) purified by chromatography on silica gel (ethyl acetate/dichloromethane, 4:1)

(b) purified by kugelrohr distillation

(c) purified by chromatography on silica gel (ether/hexane), 4:1)

Compounds 4 and 6b are commercially available (Janssen Chimica). Salts 6a(4), 6c(6) and 6d(7) are known compounds and have been prepared from the corresponding dibromides.

Example of preparation :

Ethyl N-carbomethoxy 2,3-dehydro proline 5b

A suspension of 15 mM of 3, 10 mM of salt 6b and 20 mM of dry potassium carbonate in 1,2-dimethoxyethane (5ml/g 6b) was stirred at 85°C for 8 H. After the reaction mixture was cooled, the same volume of water was added and the solution was extracted with dichloromethane. The solvent was removed at reduced pressure. The residue was extracted with ether and the product was purified by kugelrohr distillation.

References and notes

(1) J.P Bazureau and M. Le Corre, accompanying paper.

(2) A. Salomon, J. Prakt. Chem.,9,292,(1874).

(3) Isocyanate 2 was obtained by the method described by A.J. Speziale and L.R. Smith, J.Org. Chem.,27,3742,(1962),

(4) M. Le Corre, Bull. Soc. Chim. France,1951,(1974).

Recently, the ylid corresponding to this salt has been employed as precursor for 3-hydroxypyrroles(5).

(5) W. Flitsch, K. Hampel and M. Hohenhorst, Tetrahedron Lett.,4395,(1987).

(6) A. Mondon, Ann.,603,115,(1957).

(7) A. Hercouet and M. Le Corre, Tetrahedron Lett.,5,(1979).

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