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CONVERSION OF PROTECTED SERINE AND THREONINE TO CORRESPONDING DEHYDROAMINO ACIDS UNDER MILD CONDITIONS

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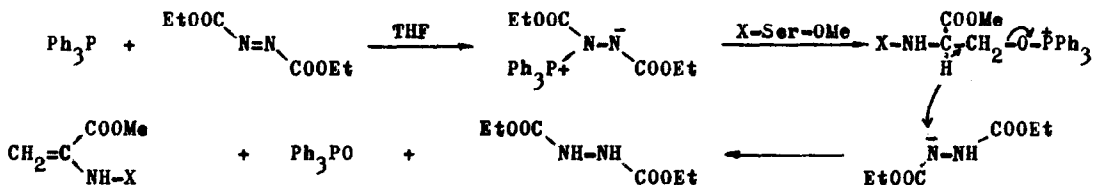
Dehydroamino acids are important constituents of certain peptide antibiotics[1]. Recently, the synthesis of dehydroalanine and 2-acylaminocrotonate derivatives was described[2]. Serine and threonine derivatives have been converted by chlorination reaction with phosphorus pentachloride and subsequent elimination, using a tertiary amine as a base to corresponding dehydroalanines and 2-acylaminocrotonates respectively. It was also reported, that triphenylphosphine and diethyl azodicarboxylate is useful for intermolecular dehydratation reaction of certain hydroxycompounds[3].

In this paper we reported application of this method for preparation of dehydroamino acids from derivatives of serine and threonine. For the protection amino groups in these amino acids, we used benzyloxycarbonyl/Z/, phtaloyl/Pht/, t-butyloxycarbonyl/Boc/, while methyl groups were employed as carboxyl protective group.

We have observed, when an appropriate hydroxyamino acid derivative are allowed to react with equimolar amounts of triphenylphosphine and diethyl azodicarboxylate corresponding dehydroamino acids are formed in 55-69% yields. /see table 1/



In case of methyl 2-benzyloxycarbonylaminocrotonate a mixture of geometrical isomers /Z and E/ were obtained. The proportion of geometrical isomers formed and assignment of configuration was determined by NMR spectroscopy. The NMR spectrum of the product mixture indicated proportion of isomers in a 50:50 /E:Z/ ratio.

In our opinion this synthesis of protected dehydroamino acids is more convenient than other methods described earlier[2].

A typical experimental procedure for converting of protected serine and threonine to corresponding dehydroamino acids by this method is described below.

To 4,1 mmol of N-protected serine or threonine[a] methyl ester dissolved in 15 ccm tetrahydrofuran, 4,1 mmol /1,07g/ of triphenylphosphine and 4,1 mmol /0,71g/ of diethyl

azodicarboxylate were added and magnetically stirred for about 4 hrs. Then solvent was removed from the reaction mixture under reduced pressure. Oily residue was dissolved in benzene and white precipitate of N,N'-diethoxycarbonylhydrazine was filtered off. The filtrate was charged on a silica gel column. The column was rinsed with benzene /if X=Pht,Z/ or hexane-diethyl ether /30:1 if X=Boc/ as eluents. Fractions containing protected dehydroamino acids were evaporated to dryness and crystallized from diethyl ether-hexane.

Table 1. Analytical data of protected dehydroamino acids[b/]

X-ΔAla-OMe				CH_3CH=C/NHX/-COOMe
X	Pht=	Z-	Boc-	Z-
yield %	65	63	69	55
m.p./°C/	111-112	36-37	oil	70-72
NMR, δ	$CDCl_3$	$CDCl_3$	CCl_4	$CDCl_3$
OCH_3	3,7	3,6	4,0	3,6
vinyl	5,9; 6,6	5,6; 6,1	5,8; 6,4	1,7-2,0/β-CH_3/; 6,5; 6,7
X	7,7	5,0; 7,2	1,7	5,1; 7,3
NH	-	7,1	7,1	7,3

a/ DL-threonine was used

b/ acceptable analytical data / ± 0,3% for C,H,N/ were obtained on all compounds

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