Transformation of β-Chloro-L-alanine Peptides into L-Cysteine Peptides

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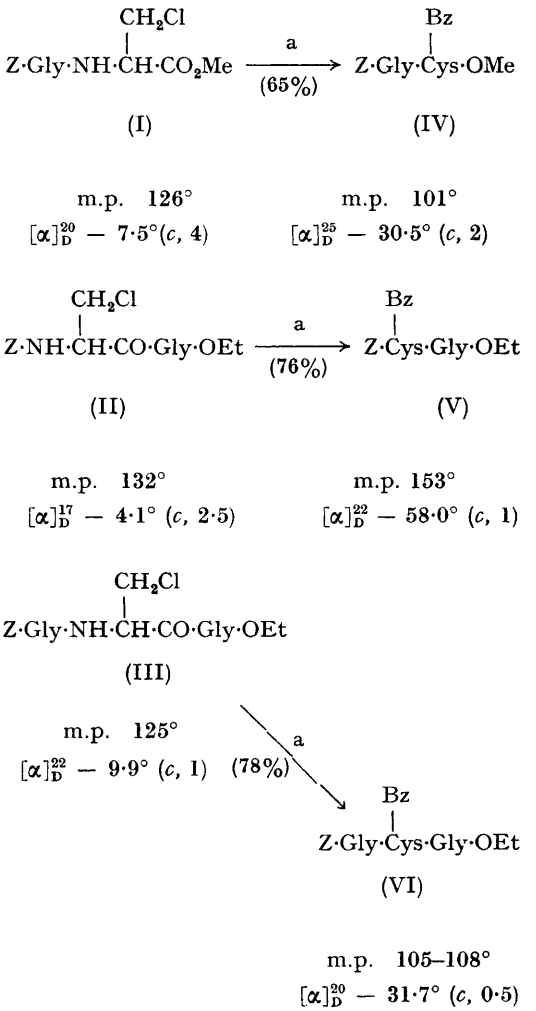
As has been previously stated[1] an alternative to the direct incorporation of *S*-protected cysteines into a peptide chain is the incorporation of *O*-substituted serine or β-halogeno-alanine residues into the chain, followed by their conversion into protected cysteine residues. In the meantime examples of transformation of L-serine into L-cysteine *via* the *O*-toluene-*p*-sulphonylserine derivatives have been reported.[2,3]

This paper deals with the conversion of β-chloro-L-alanine residues, incorporated in a peptide chain, into *S*-protected L-cysteine residues. Using as starting material β-chloro-L-alanine and its *N*-benzyloxycarbonyl derivative,[4] the peptides (I), (II), and (III) were synthesized[5] by the usual methods. By the action of potassium thiobenzoate at room temperature all these peptides were converted into the corresponding *S*-benzoyl-L-cysteine peptides (IV—VI). In a similar manner using triethylammonium thioacetate in place of potassium thiobenzoate, peptides (II) and (III) were transformed, respectively, into *S*-acetyl-*N*-benzyloxycarbonyl-L-cysteinylglycine ethyl ester (m.p. 134°; lit.,[6] gives m.p. 135—136°) and *S*-acetyl-*N*-benzyloxycarbonylglycyl-L-cysteinylglycine ethyl ester (m.p. 93—95°; lit.,[2] gives m.p. 92—95°). All these transformations of β-chloro-L-alanine peptides into the corresponding *S*-acyl-L-cysteine peptides occur without racemisation. The removal of the *S*-acyl groups can be effected as usual by methanolysis.[6]



Z = $PhCH_2\cdot O\cdot CO$; Gly = $HN\cdot CH_2\cdot CO$

Cys = $\begin{matrix} CH_2S \\ | \\ HN\cdot CH\cdot CO \end{matrix}$ Bz = Ph·CO;

"a" is the reagent PhCOSK–DMF, values in parentheses beneath arrows indicate percentage yield. DMF = dimethylformamide in which values of *c* are measured.

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[1] L. Zervas and I. Photaki, *Chimia* (*Switz.*) 1960, **14**, 375.
[2] I. Photaki and V. Bardakos, *Experientia*, 1965, **21**, 371; *J. Amer. Chem. Soc.*, 1965, **87**, 3489.
[3] C. Zioudrou, M. Wilchek, and A. Patchornik, *Biochemistry*, 1965, **4**, 1811.
[4] As the dicyclohexylammonium salt, m.p. 155° (decomp.), $[\alpha]_D^{17}$ + 24·3° (*c*, 2·5, dimethylformamide).
[5] The new crystalline compounds (I), (II), (III), and (IV) gave satisfactory elemental analyses and were homogeneous by thin-layer chromatography on Silica Gel G.
[6] L. Zervas, I. Photaki, and N. Ghelis, *J. Amer. Chem. Soc.*, 1963, **85**, 1337.