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# DEAMINATIONS OF L-VALINE AND L-VALINE BENZYL ESTER

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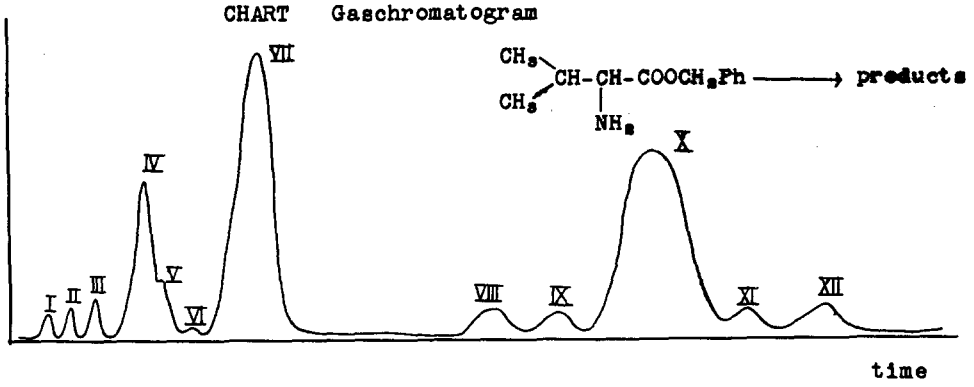
There are extensive reports on the deaminations of α-amino acids and their esters, and the deaminations of α-amino acids are generally recognized to occur with retention of configuration due to the participation of the neighboring carboxylate group, while the deaminations of α-amino acid esters proceed with racemization together with an excess inversion about the α-carbon atom.[1] Detailed examination of nitrous acid deamination of L-phenylalanine ethyl ester in acetic acid, however, revealed that various rearranged and elimination products were obtained along with the corresponding α-acetoxy ester having 11% net inversion of configuration.[2] Since optically active α-amino acids are easily available, it is of interest to examine the stereochemistry of the deaminations of optically active α-amino acid esters. This paper deals with an extension of this reaction to the β-substituted aliphatic amino acid ester, L-valine benzyl ester. The deamination of L-valine benzyl ester has been briefly reported, but not in detail.[3]

To the solution of L-valine benzyl ester ( $[\alpha]_D^{27}$ + 12.1°(1.740, dioxane)) in acetic acid was added 1.2 - 1.3 molar equivalents of sodium nitrite in portions for about 5 hours at 20 - 28°C. After standing overnight a mixture of neutral reaction products was obtained by working up as usual. GLC analysis of this reaction mixture gave 12 peaks as shown in the Chart ( 4.5 m. 3-5% carbowax 20M on Diasolid L at a column temperature of 176°C ).

The structures of each peak were identified in the following manner. Compounds III, IV, VII, VIII, IX and X were isolated from the reaction mixture and identified with authentic samples by means of IR and NMR spectra as well as

GLC technique. Compound III ( $[\alpha]_D^{23}$ - 5.9°(5.310, benzene)) was proved to be 21% net inversion of configuration by leading it to methylethylacetic acid of known configuration[4] upon catalytic hydrogenation. Compound IX ( $[\alpha]_D^{29}$ + 6.6°(2.342, benzene)) was also found to be 16% net inversion of configuration by comparison with an authentic sample. Although the isolation of V, XI and XII was unsuccessful, the mixed portion of XI and XII was shown to be a mixture of diastereoisomers of benzyl 2-methyl-3-acetoxybutyrate by comparison with a synthesized diastereoisomeric mixture of authentic samples. V was identified

CHART Gaschromatogram

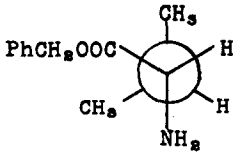



TABLE

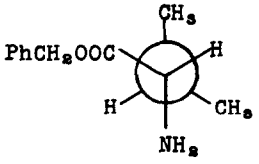
| No. | Structures | Product ratio(%) | No. | Structures | Product ratio(%) |
|---|---|---|---|---|---|
| I | unidentified | | VII | $CH_3$ $CH_3$ >C=CH-$COOCH_2Ph$ | 22 |
| II | unidentified | | VIII | $CH_3$ $CH_3-C-CH_2-COOCH_2Ph$ OH | 5-6 |
| III | $CH_2=CH-CH-COOCH_2Ph$ $CH_3$ | 1-2 | IX | $CH_3$ $CH_3$ >CH-CH-$COOCH_2Ph$ OAc | 2-3 |
| IV | $CH_2=C$ $CH_3$ $CH_2-COOCH_2Ph$ | 5-6 | X | $CH_3$ $CH_3-C-CH_2-COOCH_2Ph$ OAc | 55 |
| V | $CH_3$ $COOCH_2Ph$ >C=C< H $CH_3$ | 0-1 | XI XII | $CH_3-CH-CH-COOCH_2Ph$ AcO $CH_3$ | 6-7 |
| VI | unidentified | | | | |

to be benzyl angelate by comparison with an authentic sample by means of GLC technique. The existence of benzyl tiglate, a trans-isomer of V, could not be confirmed. The amounts of unknown compounds in three other peaks, I, II and VI, were too small to be identified. The average ratio of the products is shown in the Table.

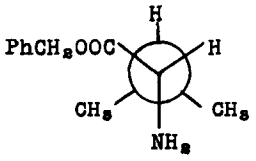
Three conformations (a), (b) and (c) are suggested for the starting amino acid ester in the stereochemistry of this reaction.




(a)

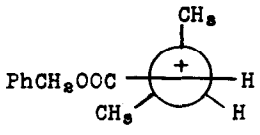



(b)

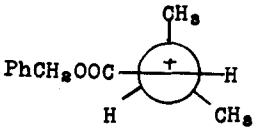



(c)

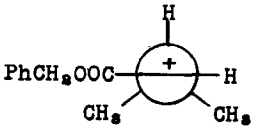
It should be noted that large amounts of tertiary β-hydrogen elimination and migration products, IV, VII, VIII and X, are observed. Considering the concerted mechanism with the loss of nitrogen, they must be produced only from conformation (c). However, (c) can not be expected to be populated to such a large extent. Then the open carbonium ion mechanism would participate in forming IV, VII, VIII and X ; that is, the initially formed (d) and (e) by way of diazonium ion followed by the loss of nitrogen would rotate to give (f),




(d)




(e)




(f)

which undergoes hydrogen migration and elimination. As previously mentioned, III and IX were obtained with 21% and 16% net inversion of configuration, respectively. Therefore, the methyl migration and the substitution to form III and IX can not be explained to occur either only by the open carbonium ion mechanism ( with racemization ) or only by the concerted diazonium ion mechanism ( with complete inversion ). Moreover, V can not be formed by the latter

mechanism. It, thus, seems most reasonable that both the open carbonium ion mechanism and the concerted diazonium ion mechanism will participate in the deamination of L-valine benzyl ester.

Although the deamination of L-valine has already been reported,[3,5] we reinvestigated this reaction under conditions similar to those described above. The product was led to benzyl ester with phenyldiazomethane and the unrearranged substitution product IX ( $[\alpha]_D^{20}$ - 39.7°(2.114, benzene)) was found to be almost only a product by GLC analysis, and moreover with at least 94% net retention of configuration. The deamination of 3-methyl-2-butylamine[6] was reported to give a different pattern of products from that of the present L-valine and L-valine benzyl ester.

Even though the carboxylate group is considered to have a so-called "holding effect", there seems as yet to be no clear explanation about the differences among the ester, carboxyl and methyl groups. We are now pursuing the clarification of properties of carbonium ions adjacent to the carboxylic acid derivatives.

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## References

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