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THE MASS SPECTRA OF *CYCLO*-TRIPEPTIDES OF B-ALANINE AND 3-AMINO-3-METHYL BUTANOIC ACID

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Abstract—The *cyclo*-tripeptides of B-alanine and of 3-amino-3-methyl butanoic acid have been synthesised, the latter for the first time, and structures were confirmed by elemental analysis and mass spectrometry; accurate mass measurements showed that carbon monoxide was lost from the molecular ions; prominent peaks in the mass spectrum of both cyclic peptides are otherwise consistent with those reported for α-peptides.

BOTH *cyclo*-(tri-B-alanyl)[1] (I) and *cyclo*-(tri-3-amino-3-methyl butyryl) (II) were prepared by cyclisation of the corresponding linear tripeptides, (III)[2,*] and (IV)[3,†]; (I) was also obtained via the active ester (V) and the hydrazide (VI). All the appropriate intermediates and final products analysed correctly.

$$\overline{[NH\cdot C(R^1)_2\cdot CH_2\cdot CONH\cdot C(R^1)_2\cdot CH_2\cdot CONH\cdot C(R^1)_2\cdot CH_2\cdot CO]}$$

(I) $R^1 = H$
(II) $R^1 = Me$

$$NH_2\cdot C(R^1)_2\cdot CH_2\cdot CONH\cdot C(R^1)_2\cdot CH_2\cdot CONH\cdot C(R^1)_2\cdot CH_2\cdot CO\cdot R^2$$

(III) $R^1 = H$, $R^2 = OH$
(IV) $R^1 = Me$, $R^2 = OH$
(V) $R^1 = H$, $R^2 = OTcp$[a]
(VI) $R^1 = H$, $R^2 = N_2H_3$

[a] Tcp = 2,4,5-Trichlorophenol

It is known that cyclo-dimerisation of linear peptides can readily occur.[4] The low resolution mass spectra of the *cyclo*-peptides (I and II) were examined to ascertain whether this in fact had happened. Molecular ions *m/e* 213 and 297 corresponded to the expected values for I and II, respectively. There was no evidence for higher molecular weight derivatives. In both cases, however, prominent ions corresponding to $[M - 28]^{+\cdot}$ were observed. Metastable peaks *m/e* 160·7 and *m/e* 243·5 provided evidence for decomposition of the molecular ions of I and II to peaks corresponding to *m/e* 185 and 269, respectively.

The $[M - 28]^{+\cdot}$ ion derived from the B-alanyl derivative (I) may be ascribed to loss of ethylene or carbon dioxide from the molecular ion; in the case of the *cyclo*-peptide (II), the $[M - 28]^{+\cdot}$ ion cannot be due to the loss of ethylene and may be rationalised as loss of carbon monoxide.

Cleavage of α-peptide residues at the CO—N bond gives rise to acylium ions, which readily lose carbon monoxide leaving a mesomerically stabilised acyliminium ion;[5] the absence of such $[M - 28]^{+\cdot}$ peaks from the spectra of B-alanyl, B-aspartyl, γ-glutaminyl and B-lysyl peptides has been recommended as a criterion for distinguishing α from ω-linked peptides.[5]

Accurate mass determinations for the ions *m/e* 213, 185 from the peptides I and

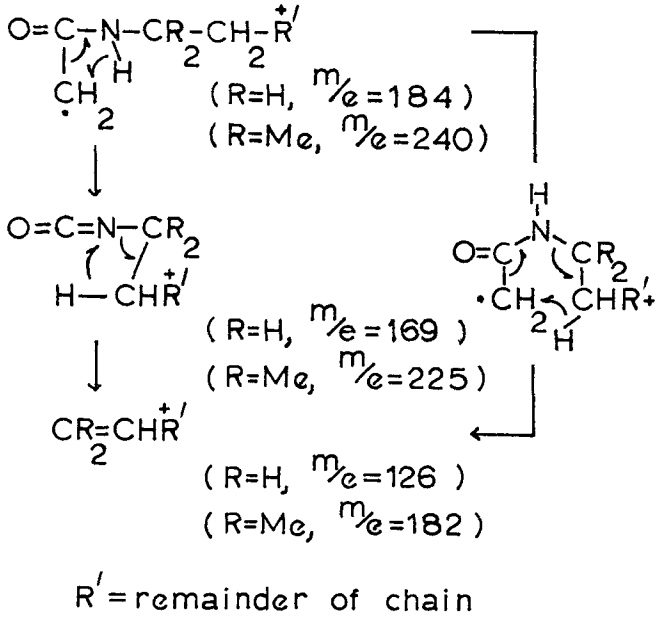
* Previously isolated as the hemi-hydrate, obtained as the mono-hydrate.
† From the benzoyl tripeptide[3] by electrolytic reduction.

III and *m/e* 297, 269 from the *cyclo*-peptide (II), respectively, have shown that the loss of the 28 fragment corresponds to the loss of carbon monoxide in each case.

It seems therefore that the absence of $[M - 28]^{+\cdot}$ peaks as a criterion for the recognition of non α-peptidic bonds is equivocal.

Prominent peaks in the mass spectrum of both cyclic peptides are otherwise consistent with fragmentation pathways reported for α-peptides.[6]

The mass spectrum of the *cyclo*-aminobutyryl derivative (II) gives rise to strong peaks at *m/e* 182 and 83 (−1 series).[6] Metastable peaks at *m/e* 210·9 and 147·2 indicate that the fragment of *m/e* 182 arises via fragments *m/e* 240 and 225—a feasible mechanism (Scheme 1) depends on the ring having opened with loss of an amine fragment; additionally, analogous precursor peaks of the *m/e* 83 fragment also appear. A similar fragmentation pathway can be discerned for the B-alanyl derivative (I).



SCHEME 1

EXPERIMENTAL

Mass spectra were obtained with 70 eV on an AEI MS-902; the samples were introduced at 225°.

The measured masses were within 5 ppm of the calculated values.

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