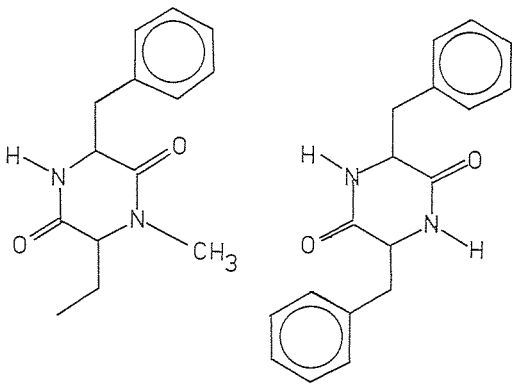
03.2-18 CYCLIC DIPEPTIDES CONTAINING ARYLMETHYL SIDE CHAINS. CONFORMATION AND STRUCTURE OF cyclo(N-METHYL-L-α-AMINOBUTYRYL-L-PHENYLALANYL) AND cyclo(L-PHENYLALANYL-L-PHENYL-ALANYL). By M. Gdaniec, Institute of Chemistry, A. Mickiewicz University, 60780 Poznań, Poland.

^{1}H and ^{13}C NMR studies as well as X-ray analysis showed that the preferred conformation of the arylmethyl side-chain in cyclic dipeptides is one in which the aromatic ring faces the 2,5-diketopiperazine ring, which represents the cyclic dipeptide backbone.
In the case of c(N-Me-L-Abu-L-Phe) there is a competition between the aliphatic and aromatic side-chains to share the space over the DKP ring. N-Methylation at the aliphatic side makes the form with the aliphatic side-chain extended to N less favorable so the form with the aliphatic side-chain facing the DKP ring becomes the major contributor. The question arises if there is enough space for both, the aromatic and aliphatic side-chains, over the DKP ring.
c(N-Me-L-Abu-L-Phe) crystallizes in space group $P2_1$ with two dipeptide molecules in an asymmetric unit. The structure was solved by application of direct methods and refined by full-matrix least-squares calculations to a final R = 0.048.
The two crystallographically independent molecules have a similar conformation. Both side chains share the space over the DKP ring. The DKP ring assumes a nearly planar conformation which allows the maximum interaction with the arylmethyl side chain without van der Waals contacts being disturbed.
c(L-Phe-L-Phe) contains two arylmethyl side chains which compete for the space over the DKP ring. Crystals of c(L-Phe-L-Phe) are orthorhombic, space group $P2_12_12$, Z = 4. The structure was solved by direct methods, the refinement is in progress.
Only one of the arylmethyl side-chains folds over the DKP ring while the second one is forced away from the space over the DKP ring.

Both compounds were kindly supplied by Prof. B. Liberek, University of Gdańsk.



c(N-Me-L-Abu-L-Phe) c(L-Phe-L-Phe)

03.2-19 CRYSTAL AND MOLECULAR STRUCTURE OF A TEN-MEMBERED CYCLODEPSITRIPEPTIDE.

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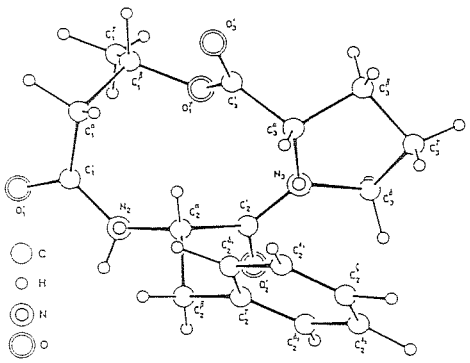
Small cyclic peptides containing one or more secondary amide bonds (-CO-NH-) are the object of increasing interest. Crucial problems concern the occurrence of transannular interactions which can lead to particular conformations stabilized by hydrogen bonds or, as in the case of cyclotripeptides, to cyclol formation.
As continuation of our studies (G. Lucente et al., J.C. S. Perkin I, 1980, 1499, and references quoted therein) on the cyclization of linear tripeptides and in order to better define the factors which favour cyclol forms over the isomeric cyclodepsipeptide and N(hydroxyacyl) diketopiperazine forms, we report here the crystal structure of a ten-membered cyclodepsitripeptide obtained by cyclization of β-hydroxy-n-butyryl-phenylalanyl-proline p-nitrophenylester.
The crystals obtained from ethyl acetate are orthorhombic with the following crystal data: S.G. $P2_12_12_1$, $C_{18}H_{22}N_2O_4$, M.W.=330.4, a=9.684(2), b=22.985(6), c=7.841(1), d_c=1.26g.cm^{-3} for Z=4.
1381 independent reflections ($I>1.5\sigma(I)$) were collected on a computer-controlled Syntex $P2_1$ four-circle diffractometer by use of graphite-monochromated Cu-Kα radiation. The structure has been solved by direct methods (MULTAN). All the hydrogen atoms were found in the final Fourier difference synthesis. The non-hydrogen atoms were anisotropically refined while the hydrogen atoms were kept fixed. The final R is 0.043.



The ω angle of the amide bond connecting the β-hydroxybutyric and phenylalanine residues is 6.6°, whereas that between the phenylalanine and proline residues is 18.1°. The lactonic bond connecting the proline residue with the β-hydroxybutyric residue is of transoid type, the torsion angle being 163.6°.
The proline ring is in a half-chair conformation with an approximate two-fold axis passing through the nitrogen atom. The benzylic side-chain of the phenylalanine residue adopts an extended conformation towards the oxygen, the N-C_α-C_β-C_γ torsion angle being -172.3°.