03. 5–15 TEN-MEMBERED CYCLOPEPTIDES: THE CRYSTAL STRUCTURE OF CYCLO(-N-METHYL-ANTRANOYL-L-PHE-L-PRO-).

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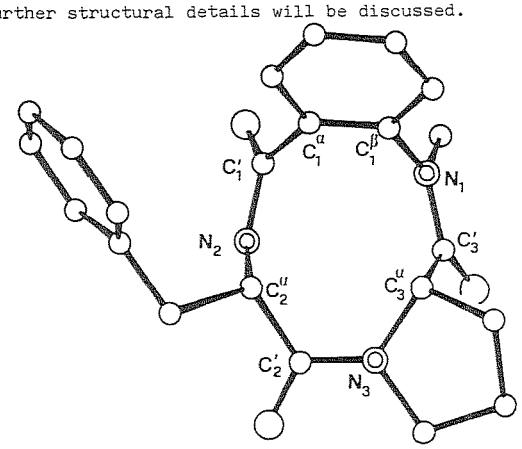
Conformational behaviour of medium sized cyclopeptides is receiving increasing attention (Kessler H., Angev. Chem. Int.Ed.,1982,21,512). These compounds are in fact good models for studying more complex biopolymers.
We previously reported on the synthesis and conformation of several peptidic cyclos, isomeric with 9-membered homodetic and heterodetic cyclic tripeptides (Lucente G., Pinnen F., Zanotti G., Cerrini S., Fedeli W., Mazza F., J. Chem. Soc. Perkin (I),1980,1499; Lucente G., Pinnen F., Zanotti G., Cerrini S., Fedeli W., Gavuzzo E., Tetrahedron Lett.,1981,22,3671; Lucente G., Pinnen F., Zanotti G., Cerrini S., Mazza F., Segre A.L., Fedeli W., J. Chem. Soc. Perkin II,1982, 1169). In continuation of our work in this field we are examining the synthesis, the conformation and the possible transannular isomerization in the less strained 10-membered rings.
As part of this program we report here the molecular structure of the 10-membered cyclic tripeptide cyclo(-N--Me-antranoyl-L-phenylalanyl-L-propyl-) obtained by cyclization of the carboxy activated linear precursor. Due to the presence in the model of the phenylalanyl and propyl residues, the possibility is also offered to study the conformation of the arylmethyl side chain and of the pyrrolidyne ring.
Crystal Data:S.G. $P2_12_12_1$, a=10.153,b=11.701,c=16.402 Å, MoKα radiation, $C_{22}H_{23}N_3O_3$, Dc=1.29 g cm^{-3} for Z=4. The current R value, for 2395 observed reflections is 0.086, calculated with the contribution of only the non-hydrogen atoms. The 10-membered ring has three "cis" peptide bonds and assumes a "boat-chair" type conformation with a pseudo-mirror plane passing through the middle points of the C_1^{α}–C_1^{β} bond and the C_2'–N_3 peptide bond. As consequence the following relationships apply to the torsion angles of the ring: $\psi_2 \simeq -\varphi_3$ $\varphi_2 \simeq -\psi_3$ $\omega_1 \simeq -\omega_3$ and $\tau(C_3'-N_1-C_1^{\beta}-C_1^{\alpha}) \simeq -\tau(C_1^{\beta}-C_1^{\alpha}-C_1'-N_2)$.
Further structural details will be discussed.



03. 5–16 NINE-MEMBERED CYCLODEPSIPEPTIDES:THE CRYSTAL AND MOLECULAR STRUCTURE OF CYCLO(-D-HYIV-L-PRO-L-PRO-).

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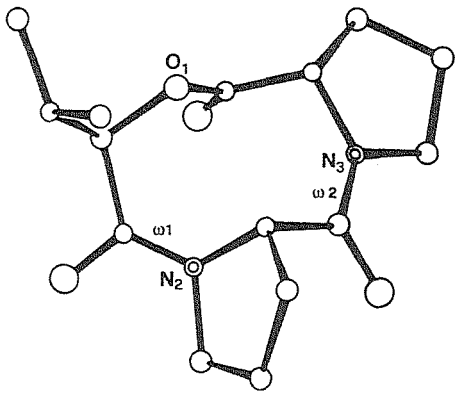
In accordance with the key role played by proline ring in the bend regions of protein chains, much work has been done on the conformation of small cyclic peptides containing proline (Deber C.M. et al., Acc. Chem. Res. 1976 9, 106). These systems are in fact good models for studying the puckering of the pyrrolidine ring and its relations with the backbone conformation (Kessler H. et al. in "Peptides", Rich D.H. and Gross E. Eds., Pierce Rockford, 1981,335). In this field we reported previously the crystal structure of the nine-membered cyclodepsipeptide cyclo(-L-HyIv-L-Pro-L-Pro-) (LLL) (Lucente G. et al. Eur.Cryst.Meeting, 1982, 189). Since in small peptides the configurational sequence of the residues strongly influences both the cyclization step and the conformation of the cyclic products, we have continued our studies with the synthesis and the cyclization of linear precursors diasteroisomeric with LLL.
Here we report the crystal structure of cyclo (-D-HyIv--L-Pro-L-Pro-) (DLL).
Crystal Data:S.G. $P2_12_12_1$,a=6.138,b=15.695,c=15.794 Å, Cu-Kα radiation, $C_{15}H_{22}N_2O_4$ D_c=1.28 g.cm^{-3} for Z=4.

The final R value, for 1216 observed reflections, is 0.050 calculated with the contribution of all the atoms.



The nine-membered ring has two cis peptide bonds with ω_1=9.3° and ω_2=-2.0° respectively and a lactonic bond of transoid type with a torsion angle of 154.4°. The two ω angles in DLL are quite different from corresponding angles found in LLL diastereoisomer, with $\Delta\omega_1 \simeq 8°$ and $\Delta\omega_2 \simeq 20°$. The conformation of the DLL ring is such that the three carbonyl groups point towards the same side of the mean plane of the nine-membered ring, while the two H(C^{α}) and the isopropilic group point towards the opposite side.