EXPERIMENTAL VIBRATIONAL SPECTROSCOPIC AND THEORETICAL (\textit{AB INITIO} CALCULATIONS) STUDIES OF THE DI-AMINO ACID PEPTIDE CYCLO(L-VAL-L-VAL)

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\textbf{Abstract:} Experimental Raman and FT-IR studies of protonated and deuteriated powder samples of cyclo(L-Val-L-Val) as well as \textit{ab initio} calculations (hybrid SCF-DFT (B3-LYP) method incorporating a cc-pVDZ basis set) have been undertaken.

The di-amino acid molecule cyclo(L-Val-L-Val), Fig.1, is an example of a peptide where the amide linkage adopts a cis conformation. There is significant scientific interest in such molecules, with respect to their use as possible antibacterial and antifungal agents \cite{1} as well as anti-tumour activity of both chelated and non chelated peptides \cite{1, 2}.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{fig1.png}
\caption{Schematic diagram of the chemical structure of cyclo(L-Val-L-Val); R = CH\textsubscript{2}CH(CH\textsubscript{3})\textsubscript{2}.}
\end{figure}

The primary focus of our studies is an ongoing research programme examining the experimental and theoretically calculated vibrational spectra (Raman and FT-IR) of cyclic and linear di-amino acid peptides. The Raman spectrum, fig. 2a, of cyclo(L-Val-L-Val) shows a weak, broad band located at 1658 cm\textsuperscript{-1} assigned to an amide I vibration. It is noticeable that on N-deuteriation this vibrational band increases in intensity and is shifted down in wavenumber by \sim 43 cm\textsuperscript{-1}. The deuterium shift is in keeping with other cyclic dipeptides investigated \cite{3, 4} and is probably typical for the N-H contribution to the potential energy distribution of the amide I mode for cyclic dipeptides adopting a cis amide conformation. For example, cyclo(L-Met-L-Met), cyclo(L-Ala-L-Ala) and cyclo(L-Ala-Gly) show an amide I shift of approximately 33, 32 and 39 cm\textsuperscript{-1} respectively.
Fig. 2. Raman spectra, in the 1400-1800 cm\(^{-1}\) region, of (a) cyclo(L-Val-L-Val) and (b) N-deuteriated cyclo(L-Val-L-Val).

The Raman band at 1491 cm\(^{-1}\) is assigned to an amide II vibration. It has been suggested previously [3] that this is not a true amide II mode and is in fact predominantly an out of phase C\(^\alpha\)-C-N stretch, with a lower degree of contribution from the N-H in plane bend than in the trans amide II mode. Indeed it can be seen (fig. 2) that the amide II band is shifted down by only \(\sim 21\) cm\(^{-1}\) after N-deuteriation. The band located at 1491 cm\(^{-1}\) is in keeping with our previous observations on cyclic di-amino acid peptides which suggest that an amide II band at wavenumbers below 1500 cm\(^{-1}\) is typical of molecules with bulky substituents on the C\(^\alpha\) atom. For example the amide II bands of cyclo(L-Asp-L-Asp), cyclo(L-Glu-L-Glu), cyclo (L-Met-L-Met), and cyclo(L-Leu-Pro) are located at 1489, 1495, 1493 and 1473 cm\(^{-1}\) respectively [4]. This is in contrast to cyclic di-amino acid peptides with smaller molecular weight substituents on the C\(^\alpha\) atom e.g. cyclo(Gly-Gly), cyclo(L-Ala-L-Ala) and cyclo(L-Ala-Gly) for which the amide II bands are observed at wavenumbers of 1517, 1523, and 1522 cm\(^{-1}\) respectively [3, 4]. Hence as the size of the amino acid side chain (R group) increases, the mass effect (possibly accompanied by an increased strain on the DKP ring) results in a decrease in the wavenumber of the amide II band (C-N stretch/N-H bend).

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References: