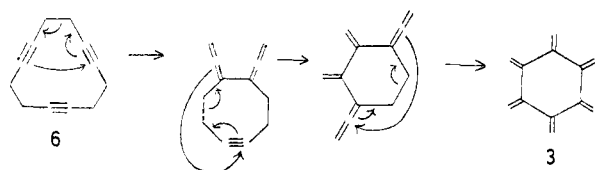


Figure 1. Calculated heats of formation (kilocalories/mole) of $C_{12}H_{12}$ isomers and butatriene using group equivalent techniques. Estimates for the xylenes and hexaradiene do not include cis-butadienoid H-H repulsions and residual aromaticity.

Scheme I



invokes a direct pathway from **6** to **3** and cannot be ruled out. Thus, a series of sequential Cope rearrangements or their equivalent as depicted in Scheme I could provide the mechanistic connection between **6** and **3**.

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β Helices Formed in Cyclohexane Solution by Oligomeric Chains of Alternating D- and L-Valine Residues. Relationship between Sequence and Prevailing Helical Sense

Sir:

Some Boc- and MeO-protected, DL-alternating oligopeptides derived from L-isoleucine and D-alloisoleucine, and having D-alle as the C-terminal residue, have been reported^{1,2} to favor in solution, independently of chain length, β -helical conformations³ with the same prevailing sense of twist. In principle, this conformational preference might be determined by the chiral side chains of identical configuration (*S*) which characterize these oligopeptides, or by the sequence pattern. In this communication we present experimental evidence from the study of similarly protected DL-alternating oligopeptides derived from valine that demonstrates that the sequence of residues in these oligomers per se can preferentially stabilize one sense of twist over the other. In addition, a correlation between the sequence pattern and the preferred handedness of the β -helical conformation is proposed.

Boc-D-Val-(L-Val-D-Val)₃-OMe (I) and Boc-(L-Val-D-Val)₄-OMe (II) were prepared using racemization-free synthetic procedures. In cyclohexane solution (25 °C) these two oligopeptides exhibit IR, NMR,⁴ and CD (Figure 1) properties similar to those observed¹ for Boc-D-alle-(L-Ile-D-alle)₃-OMe (III) and Boc-(L-Ile-D-alle)₄-OMe (IV) under the same conditions indicating that the conformational equilibria of these four oligomers in cyclohexane are analogous. In particular, since the signs of the dichroic bands (Figure 1) are identical, the handedness of the predominant β -helical conformations must be the same for all four oligopeptides. There is² some indication that the β helices formed by III and IV have \sim 4.4 residues per turn. If this, as expected, is the case also for the β helices formed by the valine oligomers, then the general arrangement of the interturn hydrogen bonds in the oligopeptides can be depicted as in Scheme I. As indicated, if the sense of twist is left-handed, the urethane NH of the octapeptides contributes to an interturn hydrogen bond, whereas that of the heptapeptides does not. The reverse is true, if the sense of twist is right-handed. The NMR spectra (360 MHz) of cyclohexane solutions of II and IV¹ show no apparent NH resonance below 6.5 ppm, while that of III⁴ shows one of the NH doublets at a substantially higher field (5.3 ppm), hinting⁵

Scheme I. Arrangement of the interturn hydrogen bonds in β helices with different sense of twist for generic Boc- and MeO-protected, DL-alternating heptapeptides (a) and octapeptides (b) having the same sequence as the oligopeptides considered in this work. β helices with 14- and 16-membered hydrogen-bonded rings (~ 4.4 residues per turn) are considered.

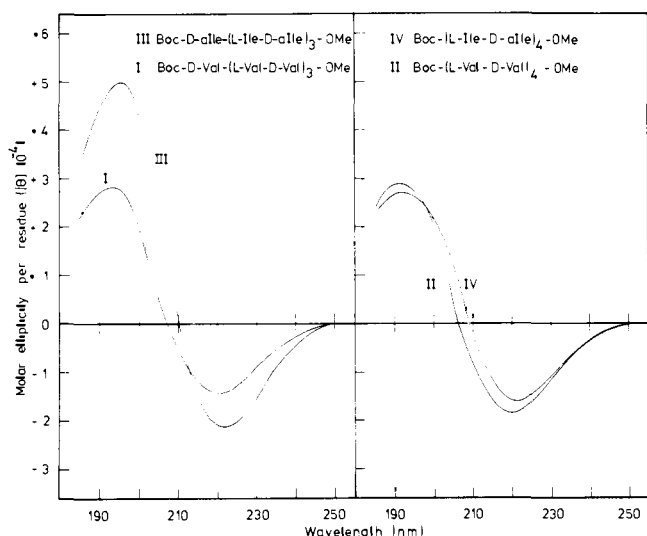
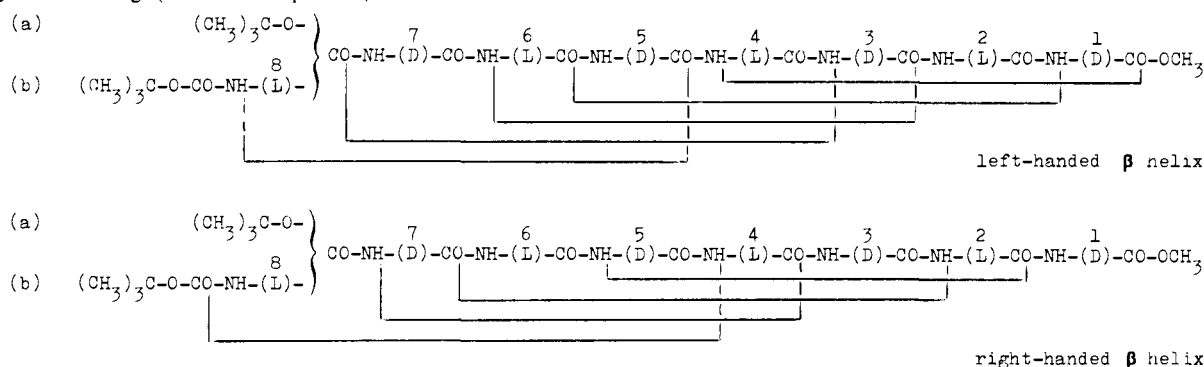


Figure 1. CD spectra of oligopeptides I-IV in cyclohexane solution: concentration, 0.2 mg/mL; T , 25 $^{\circ}\text{C}$. The ellipticity values represent the molar ellipticities of the protected oligopeptides divided by the number of the residues.

at a non-H-bonded urethane NH. Thus the NMR data strongly suggest that the predominant sense of twist is left-handed. Support for this assignment comes from Bayley's⁶ preliminary theoretical calculations of CD properties of β helices, where left-handed β helices with ~ 4.4 residues per turn have a negative ellipticity band near 200 nm and a positive one near 180 nm. The calculated positions relative to the signs of these bands coincide with those characterizing the CD spectra of Figure 1. Thus, we conclude that the predominant sense of twist of the β -helical conformations of the oligopeptides I-IV is left handed.

In the case of the alternating oligomers of DL-valine the preference for one sense of twist can only be determined by the sequence of the residues. Since the same left-handed helical sense is adopted predominantly by I and II, the preference for this particular helical sense must be related to the D residues' being in odd positions and the L-residues' being in even positions, these positions being numbered starting from the methoxy end group. It is possible that sequences of this type, with a D residue at the C-terminus, preferentially stabilize the left-handed sense, because there is one more interturn hydrogen bond for this sense than for the right-handed sense (Scheme I). III and IV have the same sequence pattern as I and II, and also favor the same handedness. Therefore, it appears likely that the sequence, and not the chirality of the side groups, is the determining factor for the preferential winding in the left-handed sense of the chains of III and IV. As long as the

nature of the side chains play only a minor role, if any, in the stabilization of a particular β -helical sense, any similarly protected DL-alternating oligopeptide having a D residue at the C-terminus should exhibit this preference for a left-handed sense for β helices in solution. Conversely, if the sequence of such oligopeptides terminates with an L residue, the right-handed sense should be favored. It is interesting to observe that a preference for the left-handed sense of twist has been proposed⁷ for the β -helical conformation of samples of poly(L-Glu(OBzl)-D-Glu(OBzl)), and can be inferred from the CD spectrum for the β -helical conformation attributed⁸ to poly(L-Ala-D-Val). Indeed, on the basis of the arguments of Heitz and Spach,⁷ the same type of relationship between sequence and the preferred sense of twist as that established for protected oligopeptides should also hold for nonprotected polypeptides.

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Reductions with Carbon Monoxide and Water in Place of Hydrogen. 1. Hydroformylation Reaction and Water Gas Shift Reaction

Sir:

When compared with the conventional method of performing the hydroformylation reaction, the Reppe modification of this process¹ reveals several features of interest and potential importance. In the normal process an olefin is converted to the next higher aldehyde or alcohol through reaction with carbon monoxide and hydrogen with use of a cobalt or rhodium carbonyl catalyst (eq 1). In the Reppe modification