polymer), 90696-54-1; $(MMB)_n$ (SRU), 90696-62-1; $(BMMM)_n$ (homopolymer), 90696-56-3; $(BMMM)_n$ (SRU), 90696-63-2.

## References and Notes


(1) Bovey, F. A. "High-Resolution NMR of Macromolecules"; Academic Press: New York, 1972.
(2) Croft, L. R. "Handbook of Protein Sequence Analysis", 2nd ed.; Wiley: New York, 1980; p 1-152.
(3) (a) Bradbury, J. H.; Crompton, M. W.; Warren, B. *Anal. Biochem.* **1974**, *62*, 310. (b) Warren, B.; Bradbury, J. H. *J. Polym. Sci., Symp.* **1975**, *No. 49*, 65.
(4) (a) Schilling, G.; Kricheldorf, H. R. *Makromol. Chem.* **1977**, *178*, 885. (b) Hull, W. E.; Kricheldorf, H. R. *J. Polym. Sci., Lett. Ed.* **1978**, *16*, 215. (c) Kricheldorf, H. R.; Mang, T., *Makromol. Chem.* **1981**, *182*, 3077. (d) Stulz, J.; Müller, D.; Hull, W. E.; Kricheldorf, H. R. *Makromol. Chem.* **1983**, *184*, 1311.
(5) Hiraoki, T.; Tsutsumi, A.; Hikichi, K.; Kaneko, M. *Polym. J.* **1976**, *8*, 429.
(6) Bamford, C. H.; Elliott, A.; Hanby, W. E. "Synthetic Polypeptides"; Academic Press: New York, 1956.
(7) Wüthlich, K. "NMR in Biological Research: Peptides and Proteins"; North-Holland Publishing Co.: 1976; Chapters 3 and 5.
(8) (a) Shoji, A.; Kawai, T.; Nishioka, A. *Macromolecules* **1977**, *10*, 1292. (b) Shoji, A.; Kawai, T.; Nishioka, A. *Makromol. Chem.* **1978**, *179*, 611.
(9) Shoji, A.; Ozaki, T.; Saitô, H.; Tabeta, R.; Ando, I. *Macromolecules* **1984**, *17*, 1472.
(10) Suzuki, Y.; Inoue, Y.; Chûjô, R. *Biopolymers* **1975**, *14*, 1223.
(11) Paolillo, L.; Tancredi, T.; Temussi, P. A.; Trivellone, E.; Bradbury, E. M.; Crane-Robinson, C., *J. Chem. Soc., Chem. Commun.* **1972**, 335.
(12) Suzuki, Y.; Inoue, Y.; Chûjô, R., *Makromol. Chem.* **1980**, *181*, 165.


# β-Helical Structure of D,L-Alternating Oligophenylalanines with Terminal Butyloxycarbonyl and Methoxy Groups in Chloroform: Comparison with Oligovalines

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ABSTRACT: This paper reports on a $^1H$ NMR study of the members II-X ($n$ = 2-10) and XV ($n$ = 15) of the series Boc-(L-Phe)$_m$-(D-Phe-L-Phe)$_{(n-m)/2}$-OMe ($n$ = number of residues in the oligopeptide; $m$ = 0 or 1) in chloroform solution at 25 °C. It is shown that there is a species that is strongly preferred by the oligophenylalanines with seven or more residues and that this species is a dimer with the structure of a right-handed $\uparrow\downarrow\beta^{5.6}$-helix with $2(n-1)$ interstrand H bonds. In the case of XV this species is virtually the only one occurring. The preference of these D,L-alternating oligophenylalanines for a $\uparrow\downarrow\beta^{5.6}$-helix contrasts with the behavior of the corresponding oligovalines, which, as it has been observed in earlier studies, form preferentially $\beta^{4.4}$-helices in chloroform. The role of the nature of the side chains in determining this different behavior is discussed.

## Introduction

There is very little in the literature[1,2] regarding the influence of the nature of the side chains on the conformational tendencies of D,L-alternating peptides. In particular, there are only hints at the possibility that the nature of the side chains may determine preferences for specific β-helical structures. We are investigating this influence by systematically studying different series of D,L-alternating cooligopeptides formed by enantiomeric or diastereomeric amino acid residues (stereocooligopeptides[3]). Here we report on a $^1H$ NMR study of the members II-X ($n$ = 2-10) and XV ($n$ = 15) of the series Boc-(L-Phe)$_m$-(D-Phe-L-Phe)$_{(n-m)/2}$-OMe ($n$ = number of residues in the oligopeptide; $m$ = 0 or 1) in chloroform solution at 25 °C and compare the results obtained with the behavior observed in earlier studies[4-7] for members of a similar series derived from valine.

## Experimental Section

**Syntheses. II-X and XV.** The oligophenylalanines II-X were synthesized following the stepwise procedure outlined in Chart I. HCl·H-L-Phe-OMe was prepared by the method of Boissonnas et al.[8] and was purified by recrystallization from MeOH/$Et_2O$: mp 160-162 °C, $[\alpha]^{20}_D$ +38.7° (c 2, EtOH) (lit.:[9] mp 159-161 °C, $[\alpha]_D$ +38.7° (c 2.9, EtOH)). Boc-D-Phe-OH, mp 85-87 °C, $[\alpha]^{20}_D$ -24.4° (c 1, EtOH), and Boc-L-Phe-OH, mp 84-86 °C, $[\alpha]^{20}_D$ +24.8° (c 1, EtOH), $[\alpha]^{20}_D$ -4.2° (c 1, AcOH) (lit.:[10] mp 84-86 °C, $[\alpha]^{18-25}_D$ -4.0° (c 1, AcOH)) were synthesized by using the di-*tert*-butyl dicarbonate method (method A)[11] and were purified by recrystallization from EtOAc/*n*-hexane. The Boc group was removed in all cases by treatment with trifluoroacetic acid. The mixed-anhydride method with isobutyl chloroformate as the mixed-anhydride-forming reagent[12] was used in each coupling step. The general procedure for the coupling reactions was the same

**Table I**
**Crystallization Solvents, Melting Points, and Elemental Analysis Data for the Oligophenylalanines II-X and XV**

| oligopeptide | recrystn solvents | mp, °C | elemental analysis[a] % C | % H | % N |
|---|---|---|---|---|---|
| II | $CHCl_3$/petroleum ether | 131-132[b] | 67.59 | 7.09 | 6.57 |
| | | | 67.56 | 6.98 | 6.53 |
| III | MeOH | 175-176 | 69.09 | 6.85 | 7.33 |
| | | | 69.00 | 6.84 | 7.30 |
| IV | MeOH/$H_2O$ | 183-184 | 69.98 | 6.71 | 7.77 |
| | | | 69.80 | 6.81 | 7.66 |
| V | MeOH | 188-190 | 70.57 | 6.62 | 8.07 |
| | | | 70.48 | 6.64 | 8.03 |
| VI | MeOH/$H_2O$ | 175-180 | 70.99 | 6.55 | 8.28 |
| | | | 70.42 | 6.43 | 8.15 |
| VII | MeOH/$H_2O$ | 190-192[c] | 71.30 | 6.50 | 8.43[d] |
| | | | 70.00 | 6.49 | 8.27 |
| VIII | $CHCl_3$/MeOH | 150-165[c] | 71.54 | 6.47 | 8.56 |
| | | | 71.04 | 6.47 | 8.48 |
| IX | $CHCl_3$/MeOH/$H_2O$[e] | >240[c] | 71.73 | 6.43 | 8.65[f] |
| | | | 70.13 | 6.30 | 8.41 |
| X | $CHCl_3$/MeOH | >240 | 71.89 | 6.41 | 8.73 |
| | | | 71.65 | 6.50 | 8.78 |
| XV | $CHCl_3$/MeOH | >240 | 72.38 | 6.33 | 8.98 |
| | | | 72.20 | 6.32 | 8.98 |

[a] First line, calcd; second line, found. [b] Lit.[14] 127-130 °C. [c] Efflorescent crystals. [d] C/N, calcd, 8.46; found, 8.46. [e] The amount of water relative to that of the other two solvents was very small. [f] C/N, calcd, 8.24; found, 8.34.

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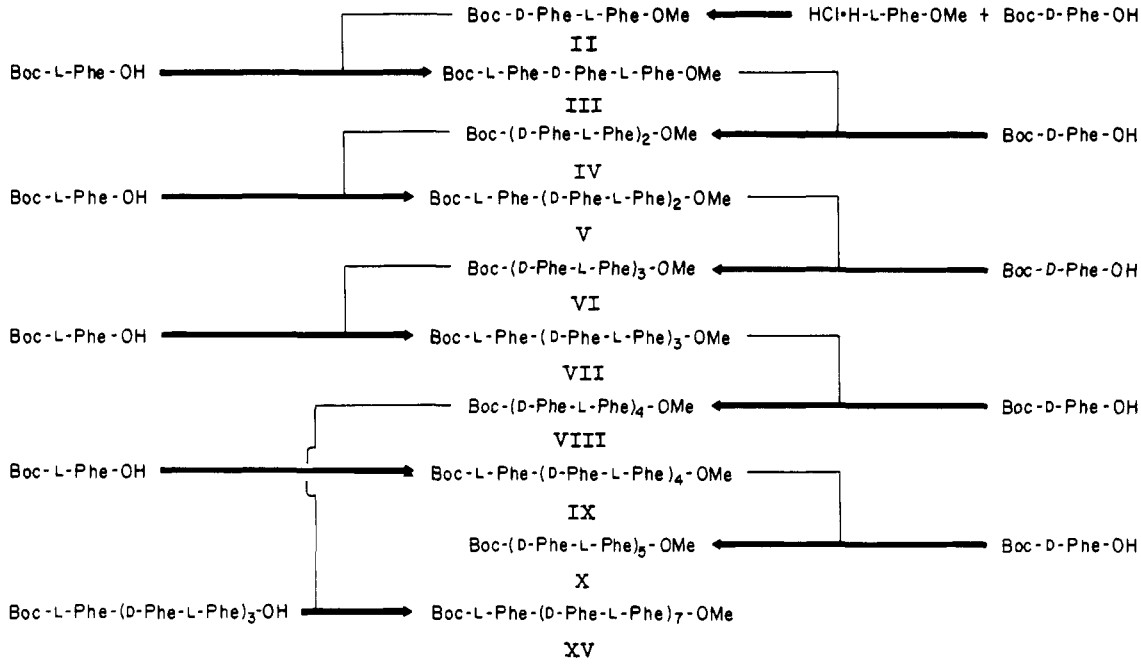
Chart I
Synthesis of the Oligophenylalanines II-X and XV[a]




[a] The thinner lines represent the deprotection steps.

as that followed in an earlier work.[13] However, in the synthesis of V–VII the peptide methyl ester was added as a solution in DMF rather than in $CHCl_3$. The workup was made by washing the reaction mixture (a solution) with 0.5 N $Na_2CO_3$, with 0.5 N HCl, and finally with water until the washings were neutral. After drying over $MgSO_4$ the solution was evaporated to dryness. The crude product obtained was purified in most cases by recrystallization. In the cases of VI, VII, and X the product was purified first by column chromatography using silica gel and $CHCl_3$/MeOH (19/1 by volume) and then recrystallized. Recrystallization solvents, melting points, and elemental analyses are given in Table I. The oligopeptides II–IV but not the higher oligopeptides gave mass spectra showing the molecular ion peak.

XV was prepared as indicated in Chart I by a fragment condensation. Boc-L-Phe-(D-Phe-L-Phe)$_3$-OH was obtained from the corresponding methyl ester VII. This (1 mmol) was dissolved in 35 mL of a mixture of $CHCl_3$ and MeOH (8/3, by volume). One milliliter of 2 N NaOH was added and the reaction mixture was stirred at room temperature for 24 h. Two milliliters of AcOH was added, and the mixture was washed with 0.5 N $Na_2CO_3$, then with 0.5 N HCl, and finally with water. After drying over $MgSO_4$ the solvent was evaporated off and the peptide acid obtained was recrystallized from MeOH/$H_2O$ (yield, 73%). The acid showed a single spot by TLC and was used without characterization. The coupling with the octapeptide methyl ester was carried out as the other coupling reactions. $CHCl_3$ was used as the solvent. After the usual workup the crude product was purified by column chromatography using the same conditions as for VI, VII, and X and recrystallized from $CHCl_3$/MeOH (Table I). We consider this final product to have a high degree of chemical and stereochemical purity on the following grounds: (i) the product gave a single spot on silica gel plates (eluent, $CHCl_3$/MeOH, 19/1 by volume); (ii) in solvents such as $CDCl_3$ (see Results) and $CD_2Cl_2$ it yielded $^1$H NMR spectra indicating the occurrence of virtually only one series of signals (Figure 1); (iii) the synthesis of monodeuterated analogues of VII by fragment condensation under conditions similar to those adopted for XV produced stereochemically pure products (see below).

**Monodeuterated Analogues.** These analogues were synthesized by using the selectively monodeuterated $\alpha$-amino acids. These were obtained by enzymatic resolution of Ac-$\alpha$-$^2$H-D,L-Phe-OH, which was prepared by the procedure of Upson and Hruby[15] and crystallized from acetic acid/petroleum ether (mp 142–144 °C; lit.[16] mp 146 °C). The degree of isotopic substitution at the $\alpha$-carbon atom of this racemic amino acid derivative was determined by $^1$H NMR with $CD_3OD$ as the solvent and found to be about 77%. The resolution was done by using hog kidney acylase I according to the literature,[16] and the hydrolysis of Ac-$\alpha$-$^2$H-D-Phe-OH was performed by refluxing with 2 N HCl for 2 h. The monodeuterated analogues $^2H^\alpha$(1)-VII, $^2H^\alpha$(2)-VII, $^2H^\alpha$-(1)-VIII, and $^2H^\alpha$(2)-VIII were prepared in the same way as VII and VIII by using the necessary deuterated Boc-amino acid at the appropriate coupling step. Boc-$\alpha$-$^2$H-D-Phe-OH and Boc-$\alpha$-$^2$H-L-Phe-OH were prepared and purified exactly as the nondeuterated analogues. The other deuterated analogues of VII were prepared as indicated in Chart II. Boc-L-Phe-D-Phe-OH and Boc-(L-Phe-D-Phe)$_2$-OH were obtained by saponification of the corresponding methyl esters, which were prepared analogously to their optical antipodes II and IV. Boc-L-Phe-(D-Phe-L-Phe)$_2$-OH was obtained by saponification of V. These acids were not characterized. $^2H^\alpha$(1)-III was obtained from II. In all cases saponification and coupling conditions were essentially the same as in the preparation of the nondeuterated compounds. HCl·H-D-Phe-OMe and HCl·H-$\alpha$-$^2$H-L-Phe-OMe were prepared by the procedure of Boissonnas et al.[8] All monodeuterated analogues exhibited $^1$H NMR spectra identical, except for the features dependent on deuteration, to those of the nondeuterated compounds, indicating a high degree of stereochemical purity.

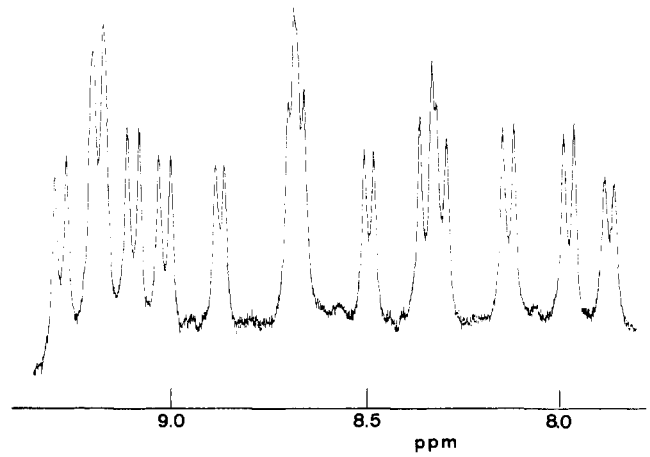


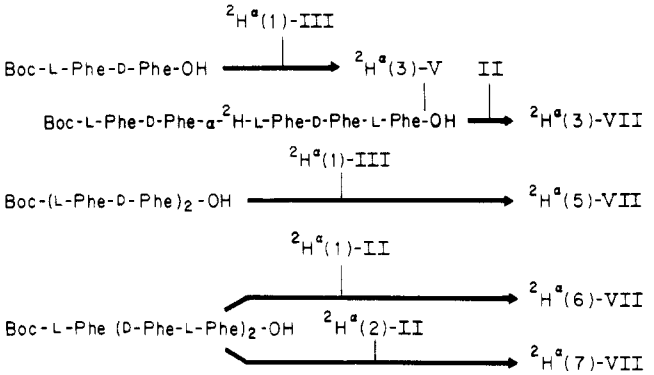

**Figure 1.** Downfield region of a $^1$H NMR spectrum of XV in $CD_2Cl_2$ (concentration, 9.4 mg/mL), showing that there is virtually only one series of NH signals. The missing NH signal (only 14 major signals are observable in the region shown) is located at higher field.

**Table II**
**Molar Mass ($M$) and Proton Chemical Shifts ($\delta$) for the Oligophenylalanines II–X and XV of the Series Boc-(L-Phe)$_m$-(D-Phe-L-Phe)$_{(n-m)/2}$-OMe ($n$, Number of Residues in the Oligopeptide; $m$, 0 or 1) Dissolved in Chloroform at 25 °C**

| | | | $^1$H NMR | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | $\delta^{a,b}$ | | | |
| oligopeptide | formula mass | $M$ | concn range, mg/mL | approx rel intens of the main set, % | Boc | $COOCH_3$ | H′(1)[c] | no. of amide-H signals below 7.5 ppm |
| II | 426.52 | [d] | 4–40 | [e] | 1.38 | 3.66 | 4.96 | 1 |
| III | 573.70 | [d] | 4–40 | [e] | 1.37 | 3.63 | 4.93–5.01[f] | 2 |
| IV | 720.87 | [d] | 6–40 | [e] | 1.35 | 3.63 | 5.05–5.18[f] | 3 |
| V | 868.05 | [d] | 4–40 | [e] | 1.32 | 3.65 | 5.14–5.30[f] | 4 |
| VI | 1015.23 | 1300[g] | 10–40 | [e] | 1.39 | 3.74 | [h] | [i] |
| VII | 1162.41 | 2200[g] | 8–110 | 95 | 1.41 | 3.91 | 5.25 | 0 |
| VIII | 1309.59 | 2700[g] | 4–40 | 90 | 1.44 | 3.91 | 6.51 | 1[j] |
| IX | 1456.76 | 2800[g] | 4–50 | 95 | 1.41 | 3.91 | 5.16 | 0 |
| X | 1603.94 | 3200[g] | 5–110 | 90 | 1.44 | 3.92 | 6.53 | 1[j] |
| XV | 2339.83 | [d] | 8–48 | 99 | 1.41 | 3.92 | ~5.1[k] | 0 |

[a] ±0.01 ppm. [b] In the case of VII–X and XV the values given are for the main set. [c] For the assignment, see text. [d] Not determined. [e] Only one set. [f] Values observed at the extrema of the concentration range indicated. [g] No significant concentration dependence was observed in the range used (5–30 mg/mL). [h] Not identified. [i] The H′ signals were very broad, and their exact number and position could not be determined. [j] Assigned to H′(2); see text. [k] Not exactly localizable because of overlapping.

Chart II
Synthesis of Some α-Monodeuterated Analogues of VII[a]




[a] The thinner lines represent deprotection steps.

**Measurements.** The $^1$H NMR measurements were performed with a Bruker HXS-360 spectrometer. The solutions were prepared at room temperature by adding 0.5 mL of solvent to a weighed amount of substance in the tube. The measurement temperature was 25 °C. All chemical shifts are relative to internal $Me_4Si$. The spin–lattice relaxation times were determined with solutions degassed via freeze–pump–thaw cycles by using the conventional inversion–recovery pulse sequence (180°–$\tau$–90°–$t$). The value of $t$ was 5 s. The $T_1$ values were calculated via a regression analysis using a single-exponential function to describe the approach of the inverted magnetization to the equilibrium value. For the analysis the program DISNMRP, 1982, Version 820601 by Bruker Instruments, Inc., was used.

The vapor pressure osmometry measurements were carried out on a Mechrolab osmometer at 25 °C. Benzil was used for the calibration. The optical rotations were measured with a Perkin-Elmer Model 141 polarimeter by using a 10-cm cell.

The melting points were determined with a Kofler melting point apparatus.

The mass spectra were measured with a Hitachi RMU-6L spectrometer using an ionizing energy of 70 eV and an inlet temperature of 80–120 °C.

The elemental analyses were done by the microanalytical laboratory of the organic chemistry institute of the ETH-Zürich.

## Results

**(a) Molar Masses.** Vapor pressure osmometry measurements were carried out for the oligopeptides VI–X dissolved in $CHCl_3$ at 25 °C. The results are given in Table II. The values found for VII–X are in each case very close to the molar mass of a dimer.

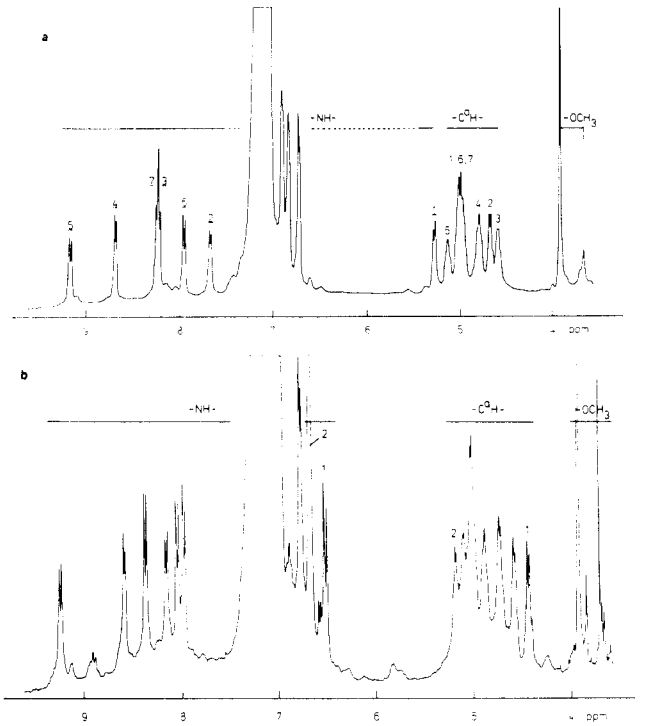



**Figure 2.** Downfield region of a 360-MHz $^1$H NMR spectrum of VII (a) and VIII (b) in $CDCl_3$. (Concentrations 109 and 14 mg/mL, respectively). The region contains all the resonances of the oligopeptide except those of the $CH_2$ protons and of the Boc group. The central group of resonances of the aromatic protons and the most intensive OMe signal are truncated. The numbers identify the H′ and H$^\alpha$ signals of various residues.

**(b) $^1$H NMR Spectra.** In $CDCl_3$, at 25 °C the lower oligophenylalanines up to the hexapeptide included yielded $^1$H NMR spectra exhibiting a single set of signals. II–V gave sharp signals, but VI gave very broad signals (for instance, the line width at half height for the resonance of the OMe protons of VI was about 20 times that of V). Starting with VII the oligophenylalanines studied yielded spectra showing a distinct, major set of signals together with other sets of signals of low to very low relative intensity. Parts a and b of Figure 2 illustrate this for the case of VII and VIII, respectively. No marked influence of the concentration on the relative intensity of these sets was observed and neither was a time dependence noted. Virtually identical spectra were obtained for a solution of

Table III
$^1$H NMR Spin-Lattice Relaxation Times for Boc-L-Phe-(D-Phe-L-Phe)$_3$-OMe (VII) and Boc-$\alpha$-$^2$H-L-Phe-(D-Phe-L-Phe)$_3$-OMe ($^2$H$^\alpha$(1)-VII) in $CDCl_3$ at 25 °C and 360 MHz

| proton | ppm | $T_1$,[a] s VII | $T_1$,[a] s $^2$H$^\alpha$(1)-VII |
|---|---|---|---|
| H$^\alpha$(2) | 4.66 | 0.47 ± 0.01 | 0.49 ± 0.02 |
| H$^\alpha$(3) | 4.58 | 0.41 ± 0.05 | 0.45 ± 0.03 |
| H$^\alpha$(4) | 4.79 | 0.50 ± 0.01 | 0.52 ± 0.02 |
| H$^\alpha$(5) | 5.12 | 0.38 ± 0.02 | 0.46 ± 0.04 |

[a] The approximations are standard deviations.

XV immediately after its preparation, after subsequent heating at 70 °C for 16 h, and also after permanence at room temperature, following this heating, for 60 days.

The most relevant spectral data are reported in Table II. For the oligophenylalanines with $n \geq 7$ only the main set of signals is considered. The assignment of the resonance of the urethane-NH proton ($^1$H′(1); we number the residues from the Boc end of the peptide chain and distinguish the backbone $^1$H′ and $^1$H$^\alpha$ protons by the sequence number of the residue to which they belong) is generally based on the position of the signal, which is the highest field one among those of the $^1$H′ protons. In the case of VII and VIII we have verified this assignment by comparing spectra of these peptides with those of the $\alpha$-monodeuterated analogues $^2$H$^\alpha$(1)-VII and $^2$H$^\alpha$(1)-VIII, respectively. The assignment of the highest field amide-H resonance to $^1$H′(2) in the cases of VIII and X (footnote *j* of Table II) is based on the spectrum of $^2$H$^\alpha$(2)-VIII and on the evidence of very strict analogies between the two peptides.

In the case of II no significant change in the position of the signals was noticed on varying the concentration, but in the case of III–V a distinct concentration dependence was observed for the position of several signals. In particular there was a sizable downfield shift of the $^1$H′ resonances upon increasing the concentration. No such concentration dependence was observed for the oligophenylalanines with $n \geq 7$, although there was some variability in the position of the $^1$H′(2) resonance of VIII (between 6.65 and 6.75 ppm) and X. Note that for these oligophenylalanines the position of the OMe signal is always at 3.91–3.92 ppm, and that the position both of the Boc and the $^1$H′(1) signal depends on whether the peptide contains an odd or an even number of residues. For VII, IX, and XV (odd $n$) the $^1$H′(1) resonance is at about 5.1–5.2 ppm, and for VIII and X (even $n$) it is at 6.51–6.53 ppm. Note also the position of the amide-H signals: whereas up to V included none of these signals is located above 7.5 ppm (approximate downfield limit of the region covered by the signals of the aromatic protons), for the oligophenylalanines with $n \geq 7$ all of them or all of them except the $^1$H′(2) resonance, depending on whether $n$ is odd or even, are located above 7.5 ppm. As far as they could be measured, the vicinal coupling constants $^3J_{H'-H^\alpha}$ for VII–X and XV were in the range 6–10 Hz.

**(c) $T_1$ Measurements.** In the case of VII we assigned individually all $^1$H$^\alpha$ resonances (Figure 2a) by using the six monodeuterated analogues $^2$H$^\alpha$(1)-VII, $^2$H$^\alpha$(2)-VII, $^2$H$^\alpha$(3)-VII, $^2$H$^\alpha$(5)-VII, $^2$H$^\alpha$(6)-VII, and $^2$H$^\alpha$(7)-VII and measured the spin–lattice relaxation times ($T_1$) of $^1$H$^\alpha$(2), $^1$H$^\alpha$(3), $^1$H$^\alpha$(4), and $^1$H$^\alpha$(5) for both VII and $^2$H$^\alpha$(1)-VII. The results (Table III) indicate that the $T_1$ value of $^1$H$^\alpha$(5) is significantly higher in $^2$H$^\alpha$(1)-VII than in VII. The $T_1$ values of the other protons are, on the other hand, virtually unaffected by the isotopic substitution on the $\alpha$-carbon atom of residue 1.

## Discussion

**(a) II–VI.** The data obtained provide only limited information on the structure of the lower oligophenylalanines in chloroform. The concentration dependence observed in the case of III–V indicates that there is some intermolecular association mediated by H bonds in the chloroform solutions of these oligopeptides. However, the extent of this association appears to be small since the $^1$H′ resonances are located generally at relatively high field. There is an increasing downfield shift of the $^1$H′ resonances with increasing chain length—this effect is shown for the $^1$H′(1) resonances in Table II—and thus it appears that associates are formed with increasing ease as the peptide chain lengthens. The broadness of the resonance lines of VI points to species of longer average lifetime than those formed by the lower oligopeptides.

**(b) VII–X and XV.** The observation of different sets of signals for the oligophenylalanines with $n \geq 7$ indicates that these peptides form species of even longer lifetime than VI. One of these species largely predominates in every case, being responsible for a set which accounts for 90% or more of the total spectral intensity (Table II). We consider the relative intensities reported for the main set in Table II as equilibrium values, since in no case were time-dependent spectral changes observed. This was checked with particular care in the case of XV (see Results, b) which presumably gives the species with the longest lifetime among the peptides investigated.

To the predominating species we attribute the structure of a right-handed $\uparrow\downarrow\beta^{5.6}$-helix with $2(n-1)$ interstrand H bonds based on the following considerations.

**Evidence for a Double-Stranded $\beta^{5.6}$-Helix with $2(n-1)$ Interstrand H-Bonds.** The molar mass values reported in Table II indicate that the species is in every case a dimer, and the high values of the coupling constants $^3J_{H'-H^\alpha}$ suggest that this dimer may be $\beta$-helical. Since the main NMR set shows only one signal for each chemically different proton or group of protons, the dimer must be made up by two symmetrically equivalent chains. Indications regarding the H-bonding characteristics of the dimer are provided by the position of the $^1$H′ resonances. In earlier NMR studies[4–6] of $\beta$-helical Boc-protected oligovalines in $CDCl_3$ at 25 °C, it was established that amide-H signals above 7.2 ppm derive from NH groups engaged in H bonding, whereas amide-H signals below 7 ppm are given by non-H-bonded groups. In the case of the oligophenylalanines studied here ring current effects may influence the spectral positions of the $^1$H′ signals, but nevertheless it seems safe to attribute amide-H signals that these peptides exhibit above 7.5 ppm to H-bonded NH groups. In the same studies[4–6] the observation was also made that the urethane-H signals are at about 6.5 or 5.3 ppm, depending on whether the urethane-NH groups are involved in H bonding or not. Thus, based on the position of the $^1$H′ resonances (Table II), in the predominating, dimeric species formed by VII–X and XV there appears to be only one NH group per chain that does not participate in H-bonding, and this is the NH(1) for VII, IX, and XV (odd $n$) and the NH(2) for VIII and X (even $n$). The only conceivable dimeric structures capable of accommodating two identical chains each with $n-1$ H-bonded NH groups are double-stranded $\beta$-helices with $C_2$ symmetry and $2(n-1)$ interstrand H bonds. $2(n-1)$ is the maximum possible number of H bonds that $\beta$-helices originated by peptides of the kind studied may have, and this number is realizable only in double-stranded helices of the highest pitch ($\beta^{5.6}$-helices). As shown by a careful analysis (Table IV) there are for every peptide three such helices possible

**Table IV**
**H-Bonding Characteristics of the Double-Stranded β-Helices with 2(n - 1) Interstrand Bonds Which Are Conceivable for Boc- and OMe-Protected, D,L-Alternating Peptides with n Residues[a]**

| n | rel arrangement of chains | helix desig | register[b,c] NH(i) | register[b,c] NH(j) | non-H-bonded NH in each chain[c] | non-H-bonded CO's in each chain[c,d] |
|---|---|---|---|---|---|---|
| odd | ↑↓ | A | CO(n + 3 - i) | CO(n - 1 - j) | NH(1) | CO(1), CO(n - 1) |
| | ↑↓ | B | CO(n + 1 - i) | CO(n - 3 - j) | NH(n - 1) | CO(n - 3), CO(n - 1) |
| | ↑↑ | C | CO(i - 3) | CO(j + 1) | NH(1) | CO(1), CO(n - 1) |
| even | ↑↓ | A | CO(n - i) | CO(n + 4 - j) | NH(2) | CO(0), CO(2) |
| | ↑↓ | B | CO(n - 2 - i) | CO(n + 2 - j) | NH(n - 1) | CO(0), CO(n - 1) |
| | ↑↑ | C | CO(i + 1) | CO(j - 3) | NH(2) | CO(0), CO(n - 1) |

[a] The helices have about 5.6 residues per turn and $C_2$ symmetry; they are right handed for peptides terminating with an L residue and left handed for those terminating with a D residue. RCO- (R = H, alkyl or aryl) and MeO-protected peptides would give helices with the same H-bonding characteristics. [b] The register is specified by the indication of the CO group of the other strand with which a particular NH of a strand is H bonded. i is odd and j is even. [c] The various groups are specified by the sequence number of the residue to which they belong. [d] CO(0) is the urethane carbonyl group.

(A–C), all with $C_2$ symmetry: two of them (A and B) are antiparallel and differ in the register of the two chains, and one (C) is parallel. The sense of twist of these helices is determined by the sequence of configurations in the peptide chains, and it is right-handed for the oligophenylalanines studied. Since the NH(1)'s (for n odd) or the NH(2)'s (for n even) are the NH groups that must be free, an antiparallel structure B with a free NH(n - 1) (Table IV) can be discarded. However, it is not possible to differentiate on this basis between the other antiparallel helix A and the parallel helix C.

**Relative Arrangement of the Chains.** In the case of VII we have determined the type of relative arrangement of the chains by using $^1$H NMR spin–lattice relaxation.[17] As Figure 3 schematically shows, the protons $^1H^{\alpha}(1)$ and $^1H^{\alpha}(5)$ are near to each other in the ↑↓$\beta^{5.6}$-helix A and far apart in the ↑↑$\beta^{5.6}$-helix C. The observation (Table III) that the $^1H^{\alpha}(5)$ has a significantly higher $T_1$ value in the deuterated analogue $^2H^{\alpha}(1)$-VII than in VII demonstrates that the two α-protons are proximate, and hence that for VII the antiparallel structure A is the correct one. The closeness of δ values observed for the OMe singlet of the oligophenylalanines with n ≥ 7 (Table II) suggests that the helix is an antiparallel helix A in all cases. That an OMe singlet at 3.91–3.92 ppm is characteristic for Boc- and OMe-protected oligophenylalanines with the structure of a ↑↓$\beta^{5.6}$-helix A is confirmed by our recent study[18] on HCO-L-Phe-(D-Phe-L-Phe)$_3$-OMe. In chloroform this formyl heptapeptide forms three major species, namely a ↑↓$\beta^{5.6}$-helix A, a ↑↑$\beta^{5.6}$-helix C and a tetramer formed by the head-to-head association of the parallel helices. The OMe singlet of the ↑↑$\beta^{5.6}$-helix C—and of the tetramer as well—is at 3.68 ppm, and therefore it is at about this position that the OMe signal of the ↑↑$\beta^{5.6}$-helix C of a Boc- and OMe-protected oligophenylalanine would be expected. It is worth noting here the influence of the N-terminal group: whereas in the case of HCO-L-Phe-(D-Phe-L-Phe)$_3$-OMe a parallel dimer is one of the major species occurring in chloroform, in the case of VII and of the other oligophenylalanines studied here, which contain the bulky Boc group as N terminus, there is a species strongly preferred and this is an antiparallel dimer.

**(c) Comparison with the Oligovalines.** The results obtained in this work show that, in chloroform, Boc- and OMe-protected, D,L-alternating oligophenylalanines, from the heptapeptide upward, have a very strong preference for a ↑↓$\beta^{5.6}$-helical structure. This behavior contrasts with that of the corresponding oligovalines which, in the same solvent, form preferentially $\beta^{4.4}$-helices.[7] This conclusively demonstrates that the nature of the side chains can determine a specific preference for a particular type of β-helix. Double-stranded β-helices of type A, B, or C (Table IV) should be always preferred if the only operative tendency would be that of maximizing the number of H bonds. That the oligovalines prefer instead $\beta^{4.4}$-helices despite the fewer H bonds, is probably due to the fact that, based on the geometric parameters reported in the literature,[19,20] these are the helices that have the $C^{\beta}$'s the least

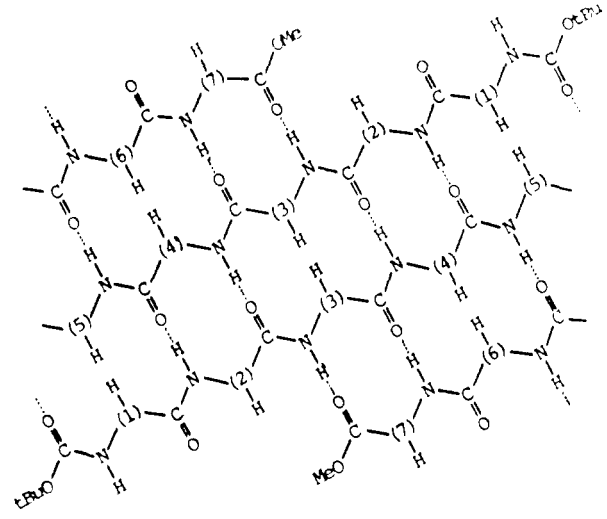



**Figure 3.** Schematic representation of the two double-stranded $\beta^{5.6}$-helices of VII which have the NH(1)'s as the only free NH groups. A is the antiparallel and C the parallel structure. The helices have been oriented with the axis parallel to the long border of the page, split along the back in this direction, opened, and flattened. The numbers give the position of the residues in the chains.

closely spaced. Therefore they may meet better than the other helices the steric requirements of the β-branched substituents of the oligovalines. These results suggest that there might be a limit to the number of residues per turn that a β-helical stereocooligo- or polypeptide can attain, and that this number might be determined by the position (and bulkiness) of the branching in the side chains. For a polypeptide such as poly(γ-benzyl glutamate), where branching is far removed from the backbone, this number might be as high as 9.0.[21]

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**Registry No.** II, 94202-58-1; $^2H^2$(1)-II, 94202-59-2; $^2H^2$(2)-II, 94202-60-5; III, 94202-61-6; $^2H^2$(1)-III, 94202-62-7; IV, 94202-63-8; V, 94202-64-9; VI, 94202-65-0; VII, 94202-66-1; $^2H^2$(1)-VII, 94202-67-2; $^2H^2$(3)-VII, 94202-68-3; $^2H^2$(5)-VII, 94202-69-4; $^2H^2$-(6)-VII, 94234-85-2; $^2H^2$(7)-VII, 94202-70-7; VIII, 85459-45-6; IX, 94202-71-8; X, 94202-72-9; XV, 94202-73-0; Boc-L-Phe-OH, 13734-34-4; H-L-Phe-OMe·HCl, 7524-50-7; Boc-yd-Phe-OH, 18942-49-9; Boc-L-Phe-(D-Phe-L-Phe)$_3$-OH, 94202-74-1; Boc-L-Phe-D-Phe-OH, 93397-22-9; Boc-(L-Phe-D-Phe)$_2$-OH, 94234-86-3; Boc-L-Phe-(D-Phe-L-Phe)$_2$-OH, 94202-75-2; Ac-α-$^2$H-DL-Phe-OH, 63570-52-5; Ac-α-$^2$H-D-Phe-OH, 81583-96-2.

## References and Notes

(1) Heitz, F.; Lotz, B.; Colonna-Cesari, F.; Spach, G. In "Biomolecular Structure, Conformation, Function and Evolution"; Srinivasan, R., Ed.; Pergamon Press: Oxford, 1980; Vol. 2, p 59.
(2) Heitz, F.; Dêtrichê, G.; Vovelle, F.; Spach, G. *Macromolecules* *14*, 1981, 47.
(3) Tomasic, L.; Stefani, A.; Lorenzi, G. P. *Helv. Chim. Acta* 1980, *63*, 2000.
(4) Lorenzi, G. P.; Jäckle, H.; Tomasic, L.; Rizzo, V.; Pedone, C. *J. Am. Chem. Soc.* 1982, *104*, 1728.
(5) Lorenzi, G. P.; Jäckle, H.; Tomasic, L.; Pedone, C.; Di Blasio, B. *Helv. Chim. Acta* 1983, *66*, 158.
(6) Lorenzi, G. P.; Jäckle, H.; Tomasic, L.; Pedone, C. *Biopolymers* 1983, *22*, 157.
(7) Jäckle, H.; Tomasic, L.; Lorenzi, G. P. In "Physical Chemistry of Transmembrane Ion Motions"; Spach, G., Ed.; Elsevier: Amsterdam, 1983; p 385.
(8) Boissonnas, R. A.; Guttmann, St.; Jaquenoud, P. A.; Waller, J. P. *Helv. Chim. Acta* 1956, *39*, 1421.
(9) Failli, A.; Nelson, V.; Immer, H.; Götz, M. *Can. J. Chem.* 1973, *51*, 2769.
(10) Schnabel, E. *Ann. Chem.* 1967, *702*, 188.
(11) Moroder, L.; Hallet, A.; Wünsch, E.; Keller, O.; Wersin, G. *Hoppe Seyler's Z. Physiol. Chem.* 1976, *357*, 1651.
(12) Vaughan, J. R., Jr.; Osato, R. L. *J. Am. Chem. Soc.* 1952, *74*, 676.
(13) Widmer, U.; Lorenzi, G. P.; Pino, P. *Biopolymers* 1979, *18*, 239.
(14) Nitecki, D. E.; Halpern, B.; Westley, J. W. *J. Org. Chem.* 1968, *33*, 864.
(15) Upson, D. A.; Hruby, V. J. *J. Org. Chem.* 1977, *42*, 2329.
(16) Birnbaum, S. M.; Levnikov, L.; Kingsley, R. B.; Greenstein, J. P. *J. Biol. Chem.* 1952, *194*, 455.
(17) Lorenzi, G. P.; Tomasic, L.; Bangerter, F.; Neuenschwander, P.; DiBlasio, B. *Helv. Chim. Acta* 1983, *66*, 2129.
(18) Lorenzi, G. P.; Gerber, C.; Jäckle, H. *Biopolymers*, 1984, *23*, 1905.
(19) Ramachandran, G. N.; Chandrasekaran, R. *Ind. J. Biochem. Biophys.* 1972, *9*, 1.
(20) Venkataram Prasad, B. V.; Chandrasekaran, R. *Int. J. Pept. Protein Res.* 1977, *10*, 129.
(21) Heitz, F.; Cary, P. D.; Crane-Robinson, C. *Macromolecules* 1977, *10*, 526.

# Structure Calculations for Silane Polymers: Polysilane and Poly(dimethylsilylene)

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ABSTRACT: The structure and conformational energies of polysilane, H–$(SiH_2)_n$–H, and poly(dimethylsilylene), Me–$(SiMe_2)_n$–Me, have been investigated by using full relaxation empirical force field (EFF) techniques. Gauche conformational states are calculated to be lowest in energy for both polymers. These results contrast with polyethylene hydrocarbon polymers which typically adopt trans conformations in the ground state. Both polysilane and poly(dimethylsilylene) are calculated to be conformationally more flexible than polyethylene.

## Introduction

Though silane polymers have been known for some time,[1] it has only been recently that moderate and high molecular weight, soluble analogues have become available.[2,3] Interest in these compounds is active for a variety of reasons: they exhibit unusual spectral properties;[4] they serve as precursors to β-silicon carbide fibers;[5] they serve as impregnating agents for strengthening ceramics;[6] and they may become semiconducting upon doping.[2d] In addition, it has recently been discovered that silane polymers may have applications in photoresist technology[7] and as photoinitiators for vinyl monomer polymerization.[8] Despite this level of interest, relatively little is known about the structural details of such polymers. While acyclic catenanes[9] of more than two silicon atoms have been the subject of several theoretical[10] and experimental[11,12] studies, the focus of many of these investigations has been on relatively short-chain silanes and permethylsilanes. As our interests[2d-i,6-8] lie mainly with the higher molecular weight polymers of silicon, we have investigated, using empirical force field (EFF) methods,[13] the structure and conformational energies of oligomers which serve as models for these polymeric compounds.[14] This paper is concerned with the results obtained for the simplest members of this class of polymer, polysilane and poly(dimethylsilylene).

## Methods

Calculations were performed by the empirical force field (EFF) method,[13] using the program MM2[16] and the full relaxation technique.[18] The silicon parameters developed for the program BIGSTRN[10b,19] for stretching and bending, which have been used previously in the program MM1,[10d,20] were employed in these calculations. Torsional parameters used in the present study are reported in ref 21. The H–Si–Si–H torsional parameter was obtained by adjusting $V_3$ until the rotation barrier[22] of 1.22 kcal/mol observed for disilane[23] was reproduced. The $C_{sp^3}$–Si–Si–$C_{sp^3}$ torsional parameter was set equal to this value[24] by analogy

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