Eur Biophys J (1985) 12:67–73

European Biophysics Journal

Molecular shape and dipole moment of alamethicin-like synthetic peptides

V. Rizzo and G. Schwarz*

Department of Biophysical Chemistry, Biocenter, University of Basel, Klingelbergstrasse 70, CH-4056 Basel, Switzerland

K.-P. Voges and G. Jung

Institute of Organic Chemistry, University of Tübingen, Federal Republic of Germany

Received August 25, 1984/Accepted in revised form February 26, 1985

Abstract. The peptides Boc-(L-Ala-Aib-L-Ala-Aib-L-Ala)$_n$-OMe, with $n=2$ (P10) and $n=4$ (P20), have been synthesized as purely hydrophobic models of the antibiotic alamethicin, which is known to be a voltage-dependent pore former in membranes and is apparently α-helical in lipophilic media. These peptides were investigated in 1-octanol, a solvent which resembles the membrane environment. From dielectric dispersion studies quantitative information on the molecular shape and dipole moments could be derived. Further independent data concerning conformation and extent of aggregation of the peptides were obtained by circular dichroism and ultracentrifuge measurements. The results suggest that the peptides assume the form of elongated particles having a significant amount of ordered secondary structure and carrying a dipole parallel to the long axis. Apparently the monomeric peptide molecules undergo, to some extent, a head-to-tail aggregation which is slightly enhanced at lower temperatures. Based on the high-frequency parts of the dielectric dispersion curves the lengths, diameters, and dipole moments of the monomer particles have been determined as 22.5 Å, 10 Å, 36 D (P10) and 28.5 Å, 12 Å, 64 D (P20).

Key words: Aggregation, dielectric dispersion, dipole moment, molecular shape, pore former

1. Introduction

Alamethicin (Meyer and Reusser 1967), trichotoxin (Brückner and Jung 1982) and other peptide antibiotics containing the α-amino-isobutyric acid residue (Aib) have been found to form voltage-dependent pores in membranes (for references see: Boheim and Kolb 1978; Hanke et al. 1983). From an analysis of experimental data obtained with black lipid membranes, it has been concluded that alamethicin pores are formed by aggregation of several (probably 6 to 10) monomeric peptide chains. These channels are usually promoted by a positive electric potential on the side of application of the peptide.

Extensive conformational studies on alamethicin and its natural and synthetic analogs have shown that the secondary structures are largely α-helical in lipophilic solution (for references see: Jung et al. 1984). This feature appears to be related in a direct way to the high Aib content of these peptides (Jung et al. 1983a). It should be emphasized that the electric dipole associated with such a conformation has been incorporated into various models proposed for the alamethicin gating process (Fox and Richards 1982; Boheim et al. 1983; Mathew and Balaram 1983; Hall et al. 1984). At the present time we shall not critically review their different proposals.

Structural information concerning the details of field induced modulation of the properties is not available. Accordingly this point is the subject of most speculations with regard to a possible gating mechanism. A thermodynamic analysis (Schwarz 1977) reveals that a field-dependent conformational equilibrium is a necessary consequence of differences in dipole moment occurring among different conformers. The apparent significance of the dipolar properties of alamethicin and related peptides prompted us to carry out dielectric dispersion measurements in solution. Previous studies have been done with alamethicin (Schwarz and Savko 1982) and trichotoxin (Schwarz et al. 1983) in octanol/dioxane, whereas melittin, another electrically sensitive pore-forming peptide (which, however, does not contain Aib) was investigated in *n*-butanol saturated with water (Sano and Schwarz 1983). In the present article we report results of dielectric measurements on two synthetic peptides (P10; P20) with the fol-

* To whom offprint requests should be sent

lowing sequences:

Boc-(L-Ala-Aib-L-Ala-Aib-L-Ala)$_n$-OMe
(P10: $n=2$; P20: $n=4$).

They, too, have been shown to induce voltage-dependent ion-conducting channels in black lipid membranes (Jung et al. 1983b). The most interesting point lies in the complete lack of ionizable or strongly polar side chains. This permits structural features and dipole moments to be interpreted in terms of main-chain contributions.

2. Materials and methods

The synthesis and chemical characterization of the peptides P10 and P20 will be described elsewhere (Voges and Jung, unpublished). 1-Octanol puriss, obtained from Fluka (Buchs, Switzerland) was redistilled under reduced pressure and stored dry. Complete dissolution into 1-octanol was achieved for both peptides, lyophilized from t-butanol, after treatment for ten minutes in a sonicator water bath (Elgasonic from Elga, Bienne, Switzerland). The concentration was routinely determined by measuring the ellipticity at 222 nm with a circular dichrograph (Cary 61). Determination of the molar ellipticity and testing the linear concentration dependence had been performed beforehand with a stock solution prepared by weight.

Dielectric dispersion measurements were carried out in the range 5 kHz to 50 MHz using three different impedance bridges: 75C and 33A/1 from Boonton Electronics (Parsipanny, N.J.) and B201 from Wayne Kerr Corp. (Montclair, N.J.). The cell and calibration details have been described before (Schwarz and Savko 1982). Data from two bridges whose frequency range did not overlap generally differed by a small constant quantity, which however never exceeded the absolute calibration error. This small difference was corrected for with a suitable extrapolation procedure.

Preliminary studies had shown that a rather peculiar increase occurred at frequencies higher than 10 MHz when the peptide contribution to the relative permittivity, ε'_{pep}, was evaluated as $\varepsilon'_{pep} = \varepsilon'_{tot} - \varepsilon'_{sol}$ (ε'_{tot}, ε'_{sol} being the corresponding permittivities of the total solution and the pure solvent, respectively). This undesired effect was traced to some contamination of the peptide solutions with small amounts of water (up to a few mg/ml) which was found to appreciably alter the dielectric relaxation properties of 1-octanol. Therefore the dependence on the water content, x, was explicitly taken into account for the solvent permittivity and dielectric loss. These were found to be well represented by a single Debye relaxation function according to the relations

$$\varepsilon'_{sol} = \varepsilon_\infty + \frac{\Delta\varepsilon_0}{1+(f/f_0)^2}, \tag{1a}$$

$$\varepsilon''_{sol} = \frac{f/f_0}{1+(f/f_0)^2}\Delta\varepsilon_0, \tag{1b}$$

where f is the applied frequency. Note that ε_∞: the high frequency permittivity, $\Delta\varepsilon_0$: the dielectric relaxation amplitude, and f_0: the relaxation frequency, depend on the water content. A careful quantitative investigation of these dielectric parameters for 1-octanol containing known small amounts of water (0 to 10 mg/ml) showed that their dependence on x could be very well described by a quadratic polynomial. In this way, the solvent contribution to ε' and ε'', respectively, became a function of a single parameter, x. A non-linear least-squares procedure (Bevington 1969) was then used to determine the value of x which produced the best Cole-Cole plot of ε''_{pep} vs. ε'_{pep} in each set of data. After such a treatment, the reproducibility of the data was comparable to that expected from the known bridge accuracy. However, because of this empirical data correction, the peptide contribution to the high frequency dielectric constant of the solution, $\Delta\varepsilon_\infty$ (see Eqn. 2 below), was rather poorly determined. Therefore this quantity is not reported nor has it been used in the discussion.

Apparent molecular weights of the solute particles were determined by equilibrium sedimentation with an analytical ultracentrifuge (Beckman, Model E) using both schlieren and interference detection methods. From density measurements the partial specific volume of the two peptides in 1-octanol was found to be $\bar{v} = 0.805$ ml/g.

3. Results

As pointed out in the experimental section, the peptide contributions to the relative permittivity, ε'_{pep}, and to the dielectric loss, ε''_{pep}, follow the Cole-Cole relation

$$\varepsilon'_{pep} - i\,\varepsilon''_{pep} = \frac{\Delta\varepsilon_0}{1+(if/f_0)^{1-\alpha}} + \Delta\varepsilon_\infty \tag{2}$$

($i=\sqrt{-1}$). This is illustrated in Fig. 1 where data obtained from solutions of the two peptides with comparable concentrations are shown to fit the Cole-Cole arc. The parameters $\Delta\varepsilon_0$ (relaxation amplitude), f_0 (dispersion frequency), α (spectral distribution coefficient of the relaxation processes), and $\Delta\varepsilon_\infty$ (peptide contribution to the high frequency dielectric constant relative to solvent) were deter-

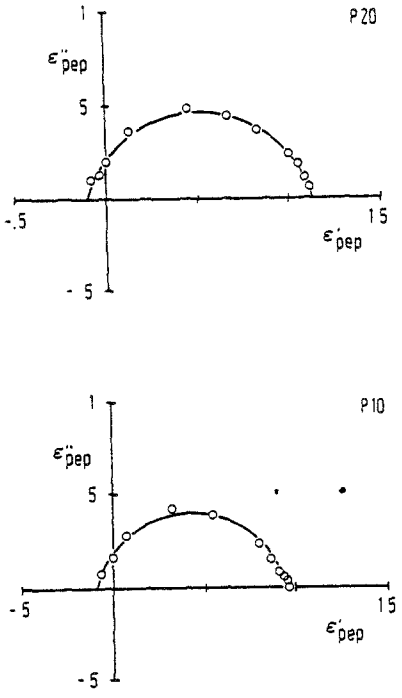

Fig. 1. Cole-Cole plots of the peptide contribution to the dielectric dispersion between 0.1 and 50 MHz. The data refer to 1-octanol solutions at 25 °C with a concentration of 5.1 mg/ml for P10 and 4.4 mg/ml for P20

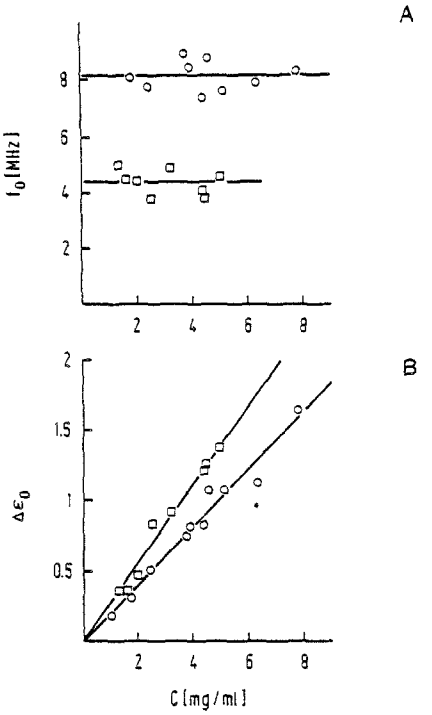

Fig. 2A and B. Concentration dependence of the relaxation frequency f_0 (**A**) and of the relaxation amplitude $\Delta\varepsilon_0$ (**B**) for the two peptides, P10 (○) and P20 (□), dissolved in 1-octanol at 25 °C

Table 1. Dielectric dispersion parameters of the investigated peptides in 1-octanol

T [°C]	P10			P20		
	$\Delta\varepsilon_0/C$ [ml/mg]	f_0 [MHz]	α	$\Delta\varepsilon_0/C$	f_0	α
10	0.249 (0.008)	4.3 (0.1)	0.12	0.307 (0.013)	2.2 (0.1)	0.14
25	0.202 (0.005)	8.1 (0.2)	0.10	0.279 (0.011)	4.4 (0.2)	0.08
40	0.170 (0.005)	15.4 (0.6)	0.10	0.263 (0.008)	8.0 (0.3)	0.08

These are concentration averaged values in the ranges 1 to 8 mg/ml for P10 and 1 to 5 mg/ml for P20 with standard deviations given in parentheses. Reproducibility of α was better than 0.05

mined using non-linear least-squares regression techniques (Bevington 1969).

No significant concentration dependence could be detected for f_0, as shown in Fig. 2A. Within the experimental accuracy, $\Delta\varepsilon_0$ was found to depend linearly on the peptide concentration in the range under investigation (see Fig. 2B). The values of f_0, α, and of the specific relaxation amplitude, $\Delta\varepsilon_0/C$, are collected in Table 1 for the two peptides dissolved in 1-octanol at three different temperatures.

As is the case with alamethicin (Schwarz and Savko 1982) and trichotoxin (Schwarz et al. 1983) dissolved in 1-octanol, the peptides P10 and P20 are not in a pure monomeric state at the concentrations used for the dielectric measurements. An estimate of the extent of aggregation can be obtained from the apparent weight averaged molecular weight, M_w, as determined in the ultracentrifuge (see Table 2). Using a simple monomer-dimer model one may calculate a lower bound of y_1, i.e. the mass fraction of the monomeric particles. The results reported in Table 2 are indeed comparable to the values observed for alamethicin and trichotoxin, respectively.

The CD spectra of the two peptides dissolved in 1-octanol (Fig. 3) indicate the presence of some secondary structure. In close agreement with the case of alamethicin (Jung et al. 1975), a pronounced negative shoulder around 220 nm, followed by a second negative peak at 207–205 nm are highly indicative of the right-handed α-helical conformation of

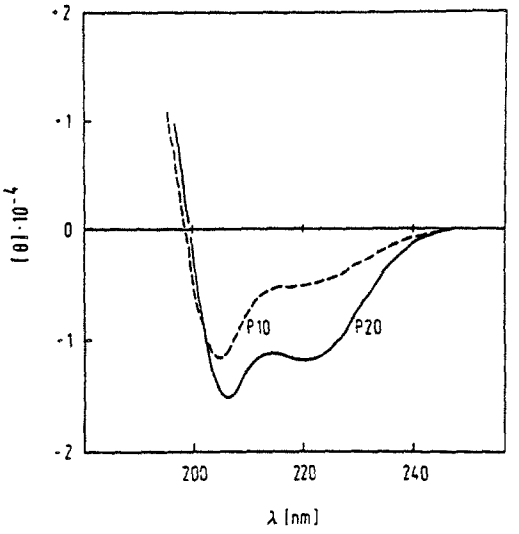

Fig. 3. Circular dichroism spectra of the two peptides, P10 and P20, dissolved in 1-octanol at 25 °C. Data were collected on solutions with a concentration of 4.6 mg/ml for P10 and of 4.4 mg/ml for P20, using a water-jacketed cylindrical cell with 0.12 mm pathlength. Molar ellipticities per residue, with units of deg cm²/dmole, are reported in the ordinates

Table 2. Results from ultracentrifuge and CD studies. (Standard deviations given in parentheses)

Peptide	M_w	M_1	y_1	$[\Theta]_{222}$
P10	1100 (50)	899	0.78 (0.05)	−4,800
P20	2400 (100)	1,666	0.56 (0.06)	−11,800

The apparent weight averaged molecular weight, M_w, was determined at 20 °C and a concentration of 6.8 mg/ml for P10, 3.3 mg/ml for P20. M_1 means the value for a monomeric particle calculated from the chemical formula. The mass fraction of monomers, y_1, is a lower bound as derived by assuming a monomer-dimer system. Molar ellipticity per residue at 222 nm, $[\Theta]_{222}$, is given in deg cm²/dmol

polypeptides. With the help of one simple published procedure (Chen et al. 1974), an estimate of the helical fraction can be determined from the experimental molar ellipticity per residue at 222 nm (−4,800 deg dmole^{-1} cm^2 for P10, −11,800 deg dmole^{-1} cm^2 for P20). With the further assumption that only one helical segment can be present in each peptide molecule, the amount of α-helical structure is calculated to be 38% for P10 and 43% for P20.

Unlike alamethicin the present peptides are not sufficiently soluble in dioxane. We could, however, prepare solutions in dioxane/octanol mixtures where the volume ratio was 1 : 2 or less. Dielectric dispersion measurements of these systems generally reflected the phenomenon already observed with the natural analogues, namely that the addition of dioxane induces a pronounced formation of large aggregate particles.

4. Discussion

4.1. Effective molecular shape and dimension

In line with our previous studies on the dielectric dispersion of alamethicin and trichotoxin, we interpret the observed relaxation process on the basis of a rotary diffusion controlled orientation of permanent dipoles which are carried by the peptide molecules. When we further assume a rigid ellipsoid of revolution as a model to approximate the hydrodynamic properties of the solute particles, the relevant geometrical parameters, namely the two semi-axes a and b (parallel and perpendicular, respectively, to the direction of symmetry), can be derived from the dispersion frequency, f_0, and the partial specific volume, $\bar{v}$. It can be shown that

$$f_0 = (kT/6\pi\eta v_0) \cdot \varphi(p) \qquad (3)$$

(k: Boltzmann's constant; η: solvent viscosity; $\varphi(p)$ = explicit function of the axial ratio, $p = a/b$; v_0 = molecular volume = $\gamma_s M\bar{v}/N_A$; M = molar mass; N_A = Avogadro's number; γ_s = empirical solvation factor) (Schwarz and Savko 1982). Because $v_0 = (4/3)\pi ab^2 = (4/3)\pi a^3/p^2$, effective values of a and b can be determined once a suitable value of γ_s has been chosen. According to this model, the dispersion frequency of peptide P10 or P20 can be interpreted in terms of the length $L = 2a$ and the diameter, $d = 2b$, of an equivalent prolate ellipsoid of revolution ($p > 1$) where the dipole is directed parallel to the symmetry axis. Based on literature data for the solvent viscosity (Mumford and Phillips 1950; Riddick and Bunger 1970), and using the monomer molar mass and the experimental partial specific volume, the resulting dimensions have been calculated as compiled in Table 3.

4.2. Effective dipole moments

The amplitude of the dielectric relaxation process, $\Delta\varepsilon_0$, is related to the permanent dipole moment, μ. For a dilute solution μ may be evaluated from $\Delta\varepsilon_0$

Table 3. Effective dimensions (length and diameter in Angstrom units) and dipole moments (in Debye units) of the investigated peptides in 1-octanol (see text)

Peptide		10 °C	25 °C	40 °C
P10	L [Å]	31.0 (0.5)	30.8 (0.5)	29.6 (0.5)
	d [Å]	9.0 (0.5)	9.0 (0.5)	9.2 (0.5)
	μ [D]	50.3 (0.6)	46.5 (0.6)	43.2 (0.6)
P20	L [Å]	38.9 (0.6)	37.7 (0.6)	37.1 (0.6)
	d [Å]	11.0 (0.6)	11.1 (0.6)	11.2 (0.6)
	μ [D]	76.3 (1.1)	74.2 (1.1)	73.8 (1.1)

The numbers in parentheses refer to the maximum deviation (±) due to a variation of the solvation factor γ_s in the range between 1.0 and 1.2

data by means of the Debye-Onsager approach (Schwarz and Savko 1982). Within this approximation the specific relaxation amplitude becomes

$$\Delta\varepsilon_0/C = N_A g \mu^2/3\varepsilon_v M k T \quad (4)$$

involving an appropriate correction factor, g, whose dependence on p and on the dielectric constant of solvent (≈ 10) and solute (≈ 2.5) has been already discussed (Schwarz and Savko 1982). ε_v is the absolute permittivity of the vacuum. Accordingly effective dipole moments of the two peptides have been calculated from the experimental values of $\Delta\varepsilon_0/C$ and monomeric molar masses. The results are presented in Table 3.

4.3. Analysis of data in terms of aggregation

The effective particle lengths according to Table 3 appear too large for a monomeric particle, particularly in the case of P10. We also note a small but significant increase of L and μ at decreasing temperature whereas d remains practically constant. These points can be readily understood once a certain extent of head-to-tail aggregation of monomeric peptide molecules is taken into account. The effective dimensions and dipole moments then turn out to be values which are averages over the distribution of monomers and possible higher aggregate forms. Apparently the aggregation becomes somewhat enhanced when the temperature is reduced. Additional information with respect to the extent of aggregation can be deduced from the sedimentation experiments.

Under these circumstances the measured dielectric relaxation curves should be composed of a number of simple Debye functions (of the types presented in Eqn. (1)) contributed by the various different aggregate dipoles. Neglecting dipolar components perpendicular to the long axes we can then assign a set of appropriate $\Delta\varepsilon_0$, f_0 to each individual aggregation mode. The dispersion frequency associated with the monomeric particles, f_{01}, is expected to be about a factor of 4 larger than f_{02}, the dispersion frequency of (head-to-tail) dimers. We may therefore assume that a single Debye function involving f_{01} and a corresponding amplitude, $\Delta\varepsilon_{01} = \beta_1 \Delta\varepsilon_0$, largely describes the dispersion data in the higher frequency range. Accordingly we arrive at $f_{01} \approx f(\varepsilon'_{pep} - \Delta\varepsilon_\infty)/\varepsilon''_{pep}$ for $f \gtrsim 20$ MHz. This yields $f_{01} \approx 15$ and ≈ 6.5 MHz as a first approximation for P10 and P20, respectively. The amplitude factor β_1 may be estimated from the original Cole-Cole plot by drawing a semicircle (representing a single Debye function) so that it approximates only the high-frequency data points. From data obtained at concentrations close to those of the ultracentrifuge

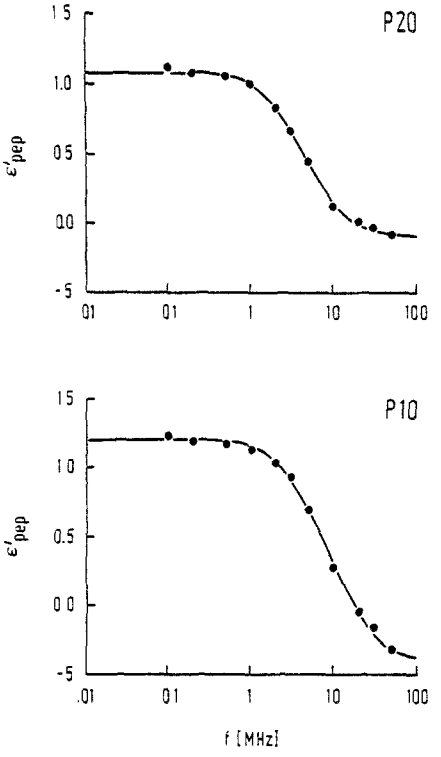

Fig. 4. Results of fitting the total peptide contribution to the solution permittivity in terms of two Debye functions. The curves plotted correspond to $f_{01} = 14.7$ MHz, $f_{02} = 3.9$ MHz and $\beta_1 = 0.58$ for P10, and to $f_{01} = 7.6$ MHz, $f_{02} = 2.7$ MHz and $\beta_1 = 0.49$ for P20

experiments we calculate $\beta_1 \approx 0.6$ (P10) and ≈ 0.4 (P20). These β_1 and f_{01} values are then used as starting points in a non-linear fitting of the total dielectric dispersion curves of P10 and P20 by means of two Debye functions. The result is illustrated in Fig. 4, where the final values of the parameters f_{01}, f_{02} and β_1 are also reported. The dimensions and dipole moment of monomeric and dimeric particles are calculated as before from Eqns. (3) and (4), after taking into account the concentration of the two species as derived from the ultracentrifuge measurements (see Table 2). We obtain for the monomeric particle:

P10: $L = 22.5$ Å $d = 10.0$ Å $\mu_1 = 36\,D$
P20: 28.5 Å 12.0 Å 64 D

with an estimated uncertainty of about 5% in the length or diameter and of about 10% in the dipole moment. Less reliable are the corresponding dimensions and dipole moments which can be calculated for the aggregate form (dimer) from f_{02} and the remaining portion of the relaxation amplitude $(1-\beta_1)\cdot\Delta\varepsilon_0$:

P10: $L = 40$ Å $d = 11$ Å $\mu_2 =$ 92 D
P20: 44 Å 14 Å 110 D.

In this case the uncertainty is due in part to the limits of a monomer-dimer model as a description of the real aggregation of the two peptides, and in part to the low abundance of the aggregated species, particularly for P10. With this caveat, a head-to-tail dimerization process explains reasonably well the trend observed on going from the monomeric to the dimeric particle: a considerable increase in length and dipole moment accompanied by only a slight change in diameter.

5. Conclusions

Quantitative analysis of dielectric dispersion data on solutions of the two peptides in 1-octanol has shown in both cases that a considerable fraction of the dipole moment of the constituent peptide bonds lies parallel to the main axis of the equivalent hydrodynamic ellipsoid, a conformationally averaged representation of the molecules. In fact, the dipole moment per residue as derived from data on the monomeric particles (3.6 *D* for P10, 3.2 *D* for P20) are close to the value (3.5 *D*) assumed for the peptide bond dipole moment on the basis of studies with model compounds (Wada 1976). Because of their CD spectra, the presence of one single conformation such as an α-helix may be excluded for both P10 and P20. Therefore, the high dipole moment cannot be explained with a full allignment of the peptide dipoles along the helical axis of the molecule. On the other hand, a substantial increase of the contribution per residue in short regular hydrogen-bonded structures (Wada 1976) is a possible compensation for the necessary loss of directional correlation in the aperiodic portions of the average structure of the two peptides. It should be pointed out, however, that other experimental evidence (Jung et al. 1984) indicates that, under suitable conditions, the peptides P10 and P20 form highly or fully helical structures. For instance, ^{13}C-NMR relaxation (T_1) data obtained with chloroform solutions of the two peptides strongly suggests a uniform α-helical structure in this medium. Furthermore, the P10-related undecapeptide Boc-Ala-Aib-Ala-Aib-Ala-Glu(OBzl)-Ala-Aib-Ala-Aib-Ala-OMe crystallizes in the α-helical conformation.

In the absence of any better definition of the conformation of P10 and P20, a useful conclusion may be derived from a direct comparison with the experimental dipole moment determined for alamethicin in 1-octanol. This latter value (75 *D*) is indeed close to that attributed here to the monomeric form of P20, a peptide with the same number of residues as alamethicin. This comparison is reassuring evidence of similar conformational properties of the two peptides and an indication that the dipolar properties of alamethicin are essentially determined by its main chain.

Acknowledgements. This work was in part supported by the Swiss National Science Foundation under grant No. 3.106-0.81. We are grateful to Mr. A. Lustig for his expert help with the analytical ultracentrifuge. We also like to thank Ms. P. Savko for her skillful technical assistance.

References

Bevington PR (1969) Data reduction and error analysis for the physical sciences, chap 11. McGraw-Hill, New York

Boheim G, Kolb HA (1978) Analysis of the multi-pore system of alamethicin in a lipid membrane. J Membr Biol 38:99–150

Boheim G, Hanke W, Jung G (1983) Alamethicin pore formation: Voltage-dependent flip-flop of α-helix dipoles. Biophys Struct Mech 9:181–191

Brückner H, Jung G (1982) Synthesis of L-Prolyl-leucyl-α-aminoisobutyryl-α-aminoisobutyryl-glutamyl-valinol and proof of identity with the isolated *C*-terminal fragment of trichotoxin A40. Liebigs Ann Chem 1982:1677–1699; and refs. cited therein

Chen YH, Yang JT, Chau KH (1974) Determination of the helix and β-form of proteins in aqueous solution by circular dichroism. Biochemistry 13:3350–3359

Fox RO, Richards FM (1982) A voltage gated ion channel model inferred from the crystal structure of alamethicin at 1.5 Å resolution. Nature (London) 300:325–330

Hall JE, Vodyanov I, Balasubramanian TM, Marshall GR (1984) Alamethicin. A rich model for channel behavior. Biophys J 45:233–247

Hanke W, Methfessel C, Wilmsen H-U, Katz E, Jung G, Boheim G (1983) Melittin and chemically modified trochotoxin form alamethicin-like multistate pores. Biochim Biophys Acta 727:108–114

Jung G, Dubischar W, Leibfritz D (1975) Conformational changes of alamethicin induced by solvent and temperature. Eur J Biochem 54:395–409

Jung G, Bosch R, Katz E, Schmitt H, Voges KP, Winter W (1983a) Stabilizing effects of 2-methylalanine residues on β-turns and α-helices. Biopolymers 22:241–246

Jung G, Katz E, Schmitt H, Voges KP, Menestrina G, Boheim G (1983b) Conformational requirements for the potential dependent pore formation of the peptide antibiotics alamethicin, suzukacillin and trichotoxin. In: Spach G (ed) Physical chemistry of transmembrane ion motions. Stud Phys Theor Chem, vol 24. Elsevier, Amsterdam, pp 349–357

Jung G, Boheim G, Bosch R, Brückner H, Hartter P, Katz E, König WA, Schmitt H, Voges KP, Winter W (1984) Primary and secondary structures of peptides which form voltage-dependent pores in lipid bilayers. In: Voelter W et al. (eds) Chemistry of peptides and proteins, vol 2. W de Gruyter, Berlin, pp 215–226

Mathew MK, Balaram P (1983) A helix dipole model for alamethicin and related transmembrane channels. FEBS Lett 157:1–5

Meyer P, Reusser F (1967) A polypeptide antibacterial agent isolated from Trichoderma Viride. Experientia (Basel) 23:85–86

Mumford SA, Phillips JWC (1950) The physical properties of some aliphatic compounds. J Chem Soc (London) 75–81

Riddick JA, Bunger WB (1970) Organic solvents. In: Weissberger A (ed) Techniques of chemistry, vol 2. Wiley Interscience, New York, p 181

Sano T, Schwarz G (1983) Structure and dipole moment of melittin molecules in butanol/water as derived from dielectric dispersion and circular dichroism. Biochim Biophys Acta 745:189–193

Schwarz G (1977) Chemical transitions of biopolymers induced by an electric field and their effects in dielectrics and birefringence. Ann NY Acad Sci 303:190–197

Schwarz G, Savko P (1982) Structural and dipolar properties of the voltage-dependent pore former alamethicin in octanol/dioxane. Biophys J 39:211–219

Schwarz G, Savko P, Jung G (1983) Solvent dependent structural features of the membrane active peptide trichotoxin 40 as reflected in its dielectric dispersion. Biochim Biophys Acta 718:419–428

Wada A (1976) The α-helix as an electric macro-dipole. Adv Biophys 9:1–63