ton transfer between imidazole and chlor phenol red (k_{43}), appears to be slightly smaller than the value expected for a diffusion controlled process.[3] Weller[8] also found similar rates for reactions with acridine ($k \sim 5 \times 10^8\ M^{-1}$ sec.$^{-1}$) which suggests that this rate either is characteristic of proton transfers involving a nitrogen atom or depends somewhat on the pK-values of the proton donor–acceptor system. For such transfer processes, diffusion controlled rates ($k \sim 3 \times 10^9\ M^{-1}$ sec.$^{-1}$) have been found[8] only when the proton was transferred between two oxygen atoms which were more acidic ($pK \sim 5$) than the systems considered above.

The value of k_{12} should be compared to previous results obtained for similar reactions between a cation and hydroxyl ion; these are listed in Table I. All these rate constants are characteristic of diffusion controlled processes; the differences in rates are due to steric factors. Thus, ammonia is the fastest because it has four sites for proton transfer. Trimethylamine ion, on the other hand, is sterically hindered by the methyl groups and has a correspondingly slower rate of reaction. The fact

TABLE I

Cation	$k_{12}(M^{-1}$ sec.$^{-1})$	Reference
NH_4^+	3.0×10^{10}	1
Acridinium	1.85×10^{10}	8
$(CH_3)_3NH^+$	1.0×10^{10}	9

that the imidazole rate constant is twice as large as that for trimethylamine indicates that the reaction is able to take place at both nitrogen atoms in the imidazolium ion ring. This occurrence is due either to resonance stabilization which makes the two nitrogens equivalent, or to a fast tautomerization of the ring after reaction at the neutral nitrogen. Acridine would be expected to be less sterically hindered than trimethylamine, but should react more slowly than imidazole, which has two reactive nitrogen atoms. This fact is in accord with the intermediate value of the rate constant that was found.

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MAX PLANCK INSTITUT FUER PHYSIKALISCHE CHEMIE
GOETTINGEN, GERMANY
MANFRED EIGEN
GORDON G. HAMMES
KENNETH KUSTIN

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CONFORMATIONAL ASPECTS OF SYNTHETIC POLYPEPTIDES. II. CRITICAL RANGE FOR INTRAMOLECULAR HYDROGEN BONDING

Sir:

In our previous report,[1] we employed optical activity to measure the conformation[2-9] of oligomeric compounds derived from γ-methyl-L-glutamic acid. The optical activities were determined in both random coil and helix-forming solvents. However, association complicated interpretation of the results.[1,10] Molecular weight determinations using short column equilibrium ultracentrifugation confirmed association.[11] In this communication we wish to report optical activity enhancements and abnormal rotatory dispersions for the oligomeric peptides in solvents where no association occurs. When the oligomeric peptides are studied in dimethylformamide and *m*-cresol, concentration independent optical activity enhancements are noted (Table II). The lack of association was confirmed by molecular weight determination in dimethylformamide.[11] Table I contains a list of the optical rotations and rotatory dispersion b_0 values from the Moffitt equation[12] for polymers of poly-γ-methyl-L-glutamates in dimethylformamide and dichloroacetic acid.

TABLE I

OPTICAL ROTATION DATA ON POLY-γ-METHYL-L-GLUTAMATES

Solvent	A/I	$[a]^{25}D$	b_0[a]
Dimethylformamide	High	+10	−544
Dimethylformamide	93	+10	−532
Dimethylformamide	22	+ 8	−486
Dichloroacetic acid	104	−33	+ 56

[a] Corrected for refractive index of solvent; a value of 212 mμ was used as λ_0.

Rotatory dispersion as a criterion for helix content has been established and examined by Moffitt,[12] Doty,[2] Cohen,[13] Tinoco,[14] Blout[15] and Elliott.[16] Moffitt expanded the Drude equation to include a higher order term.[12] He suggested that a plot of $[\alpha](\lambda^2-\lambda_0^2)$ *vs.* $(\lambda^2-\lambda^2_0)^{-1}$ with other than a zero slope exhibits abnormal rotatory dispersion, indicating helical structures. Doty[2] suggested the use of λ_c[17] as a criterion of helicity for some synthetic and naturally occurring polypeptides.

We determined the optical rotatory dispersion of the oligomeric compounds in helix and random coil solvents. In dichloroacetic acid Moffitt plots indicated material essentially of a random coil nature. In dimethylformamide, however, increasingly negative abnormal dispersions were observed in going from the trimer to the undecamer (Fig. 1) (Table II).

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(17) Derived from the square root of the slope obtained from a plot of $[\alpha]$ *vs.* $\lambda^2[\alpha]$.

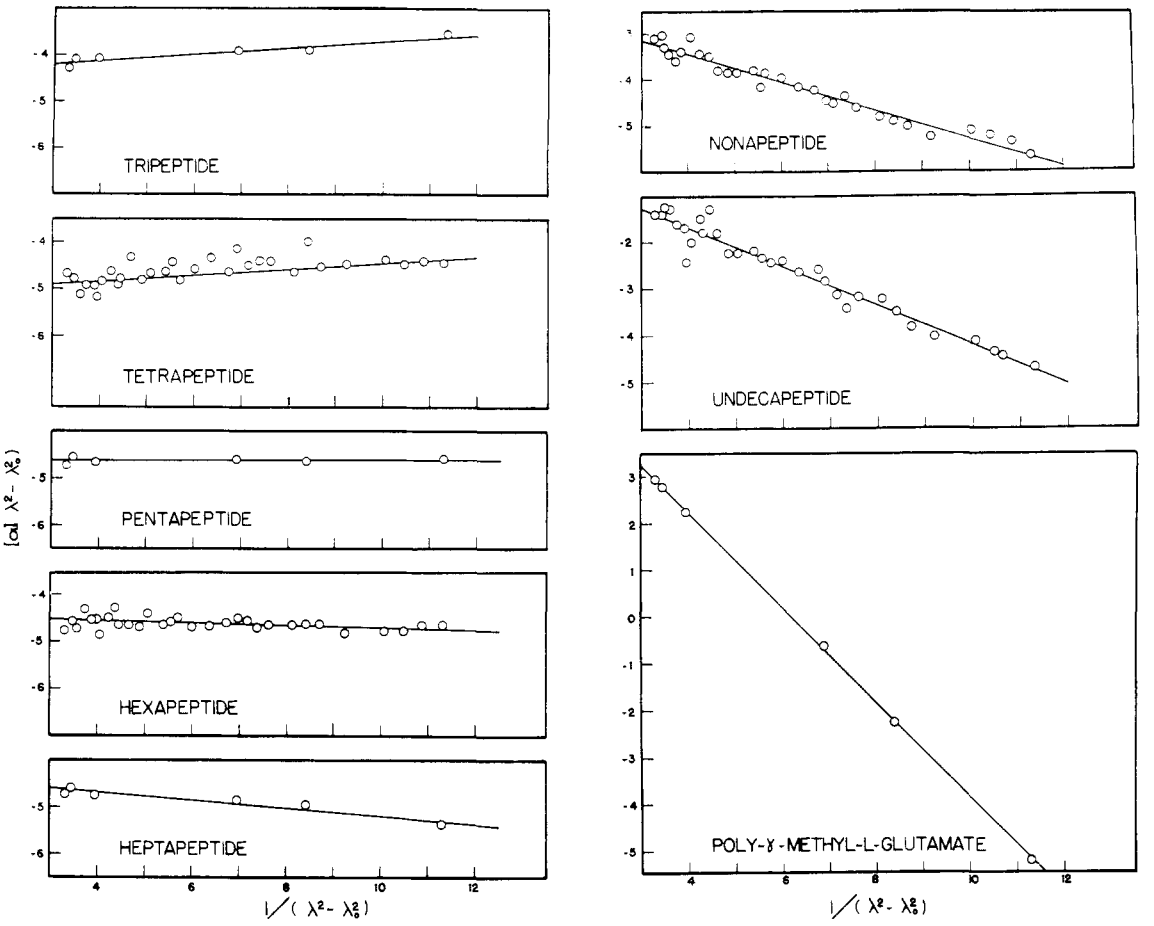

Fig. 1.—The Moffitt plots for peptides derived from γ-methyl glutamate in dimethylformamide at 25.0°

TABLE II

SPECIFIC ROTATIONS AND ABNORMAL ROTATORY COEFFICIENTS OF OLIGOMERIC PEPTIDES

No. of residues in peptide	$[\alpha]^{25}_{589}$ [a]	$[\alpha]^{25}_{589}$ [b]	b_0 [a, c]	λ_c [a]
3	−13.9	−50.0	+52	183 mμ
4	−15.7		+49	181 mμ
5	−15.5	−55.0	+4	212 mμ
6	−15.4		−18	219 mμ
7	−15.6	−50.0	−53	230 mμ [d]
9	−10.5	−37.5	−191	286 mμ [d]
11	−4.5	−14.0	−251	320 mμ [d]

[a] Taken in dimethylformamide. [b] Taken in *m*-cresol. [c] Corrected for index of refraction; a value of 212 mμ was used as λ_0. [d] Slope was not linear at higher wave lengths. Approximate values were obtained from that portion of the curve which was linear.

We feel that the abnormal optical rotatory dispersion and the optical rotation enhancement are excellent indications of stable helical forms. The critical size for helix formation in solution depends on the nature of the peptide, the solvent and the temperature.[18] For peptides derived from γ-methyl-L-glutamate in dimethylformamide at 25°, a critical range actually exists for the formation of helical structures.

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If optical activity enhancement is used as a criterion for helicity, the critical range appears to be between the hepta and nonapeptides. When the λ_c and b_0 values are used as the criteria, there seems to be a small but sudden change in these values going from the tetrapeptide to the pentapeptide while a much greater change occurs in going from the hepta- to the nonapeptide. These changes result from the folding of the peptide chain. In the region between the penta and nonapeptides intramolecular hydrogen bonds can be formed using either the carbonyl or amido groups but not both from the same amino acid residue. The large effect which commences at the nonapeptide may be attributed to more stable helical forms. At this chain length residues appear which can intramolecularly hydrogen bond both through the carbonyl and amido groups simultaneously.

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POLYTECHNIC INSTITUTE OF BROOKLYN
DEPARTMENT OF CHEMISTRY — MURRAY GOODMAN
BROOKLYN, N. Y. — EDWARD E. SCHMITT
ROCKEFELLER INSTITUTE
NEW YORK, N. Y. — DAVID YPHANTIS

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