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Studies in the Physical Chemistry of Amino Acids, Peptides and Related Substances. I. The Apparent Molal Volume and the Electrostriction of the Solvent

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The charged condition of amino acid molecules results in the orientation of solvent molecules and apparent molal volumes smaller than those characteristic of uncharged molecules.[1] Ostwald[2] long since observed that the neutralization of a strong acid by a strong base, involving the formation of water from hydrogen and hydroxyl ions, is accompanied by an expansion amounting to approximately 20 cc. per mole, and Drude and Nernst[3] calculated from data on solution volumes that the ionization of an acid or base in water produced a contraction ranging from 8 to 13 cc. per mole of substance ionized. More recently Weber[4] has studied neutralization of the amphoteric amino acids and proteins with acids and bases, and interpreted the change in volume in terms of their zwitterionic nature.

In order accurately to estimate the amount of electrostriction due to the charged groups of amino acids, peptides and proteins, we have studied the densities of a large number of amino acid compounds,[5] and considered also the measurements upon aliphatic acids, amines and amides, that had previously been measured.

I. Apparent Molal Volumes of Certain Uncharged Organic Molecules.—As a result of an extensive investigation of the apparent molal volumes of organic molecules in dilute aqueous solution Traube[6] concluded that apparent molal volumes, or molecular solution volumes, as he termed them, could be described in terms of atomic volumes. To be sure, only polar molecules are sufficiently soluble to be studied in aqueous solution. For the following elements or configurations with which we are concerned, the volumes deduced by Traube expressed as cubic centimeter per gram atom at 15° were

	C	H	N	O′		O″
Vol. of atoms, cc.	9.9	3.1	1.5	0.4	2.3[a]	5.5

	NH_2	CH_2	COOH	NH_2CH_2COOH
Vol. of groups, cc.	7.7	16.1	18.9	42.7

[a] Traube believed that a second hydroxyl group, or the second oxygen in a carboxyl group, occupied less space than the first.

The apparent molal volume calculated from these atomic volumes for NH_2CH_2COOH, the formula of the smallest of the amino acids, glycine, happens as we have elsewhere pointed out[1] to be that experimentally found. The agreement is fortuitous, for amino acids in which the positively charged ammonium group is at a greater distance from the negatively charged carboxyl group, or peptides containing more than two charged groups, exert greater electrostriction and therefore have smaller apparent molal volumes than those calculated from atomic volumes. Conversely, uncharged molecules have larger apparent molal volumes than those calculated from atomic volumes. This is presumably the result of forces which obtain not only in aqueous solution, but also in pure liquids and in the crystal lattice. Carbon atoms of adjacent molecules in the crystal lattice approach each other far less closely than those in the same molecule. It has been pointed out that this "is perhaps to be expected from the molecular nature of organic compounds, which implies differences between the intermolecular and intramolecular forces. These differences are exemplified by such physical properties as low melting points, high compressibility coefficients, etc., of molecular compounds as compared with ionic ones."[7] The melting points of the amino acids, though lower than those of salts, are higher than those of other organic compounds. x-Ray diffraction diagrams also indicate that the forces between amino acid molecules resemble those of ions rather than of uncharged molecules.[8]

Apparent Volume of the CH_2 Group.—The interatomic forces within a molecule appear not to be very different whether the organic compound is in the liquid state, or dissolved in aqueous solution. Traube contended long since that the

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(1) Cohn, McMeekin, Edsall and Blanchard, *J. Biol. Chem.*, **100** Proc. xxviii (1933).

(2) Ostwald, *J. prakt. Chem.*, **18**, 353 (1878).

(3) Drude and Nernst, *Z. physik. Chem.*, **15**, 79 (1894).

(4) Weber and Nachmannsohn, *Biochem. Z.*, **204**, 215 (1929); Weber, *ibid.*, **218**, 1 (1930).

(5) Details of preparation and criteria of purity of these compounds will be reported in subsequent papers of this series.

(6) Traube, *Samml. chem. und chem.-techn. Vortr.*, **4**, 255 (1899).

(7) Hendricks, *Chem. Rev.*, **7**, 431, 474 (1930).

(8) (a) Bernal, *Z. Krist.*, **78**, 363 (1931); (b) Hengstenberg and Lenel, *ibid.*, **77**, 424 (1931).

volume occupied by the CH_2 group is the same for pure liquids and for their aqueous solutions. Thus the apparent molal volumes of aliphatic hydrocarbons, acids and amines in the liquid state reveal an increment for each CH_2 group of between fifteen and eighteen cc. Traube's estimates of atomic volumes were made at 15°, but "the influence of temperature is so unimportant that no correction is necessary for differences in temperature of a few degrees... As the mean volume was determined from measurements on aqueous solution to be 16.1 cc. for the CH_2 group at 15°, we can approximately place the volume at 0° equal to 16.0 and at 30° equal to 16.3" (Ref. 6, p. 278).

The estimate 16.3 cc. for the volume occupied by a CH_2 group adequately describes the changes in apparent molal volume in the homologous series of acids, amines and amides considered in Table I. It is also consistent with the results of x-ray diffraction studies and the study of surface films. If the distance between the centers of adjoining carbon atoms be taken as 1.54 Å. and the angle between the valence bonds of the carbon atoms as 109°28′, the increase in length of a hydrocarbon chain is for each carbon atom: $1.54 \sin 109°28'/2 = 1.26$ Å. The distance may, of course, be somewhat larger in the liquid state, since both the angle and the distance between the carbon atoms may vary to a small extent.[9] The cross section through the carbon chain seems definitely to be greater in the liquid state than in the crystal. The volume of the CH_2 group may be related to the dimensions of the hydrocarbon chain revealed by physical measurements by the equation[10]

$$V_{CH_2} = 16.3 \text{ cc.} = 1.26 \times 21.3\ N = 1.29 \times 20.9\ N$$

where N is Avogadro's number. Adam has estimated the area of the cross section in surface films of aliphatic acids, esters, amides and urea compounds to be 20.5, of alcohols to be 21.6 and of acids on dilute HCl to be 25.1 Å.^{2} (Ref. 9, p. 50). The radii corresponding to the cross sections 20.9 and 21.3 are 2.58 and 2.61 Å.

Apparent Volume of the Terminal Groups of Aliphatic Acids.—The increment for each CH_2 group is essentially constant for the aliphatic acids (Table I). The apparent molal volume of the first member of the series, formic acid, may be taken as 34.7 cc. per mole. It contains no CH_2 group. If we assume that the CH_2 group occupies 16.3 cc. and estimate the volume occupied by the terminal groups of the other acids—in this case the H and COOH groups—we obtain (Table I) volumes which are in good agreement with that of the first member of the series, or approximately 35 cc. per mole in dilute aqueous solution. The volume apparently occupied by the terminal groups includes, to be sure, that resulting from intermolecular forces.[11]

TABLE I

APPARENT MOLAL VOLUMES OF CERTAIN OF THE GROUPS IN ORGANIC ACIDS, AMINES, AMIDES AND UREA[a]

Terminal groups	Substance	Obs. app. molal vol., cc.	Volume occupied by CONH group, cc.	Volume occupied by CH_2 group, cc.	Volume occupied by terminal groups, cc.
H + COOH	Formic acid [12]	34.7	..	..	34.7
	Acetic acid[11]	50.7	..	16.3	34.4
	Propionic acid[12]	67.9	..	32.6	35.3
	Butyric acid[12]	84.3	..	48.9	35.4
	Isobutyric acid [12]	84.5	..	48.9	35.6
	Valeric acid[13]	99.5	..	65.2	34.3
	Isovaleric acid[12]	100.6	..	65.2	35.4
	Formyl glycine[1]	70.6	20	16.3	34.3
	Formyl diglycine	107.0	40	32.6	34.4
	Formyl aminobutyric acid	104.9	20	48.9	36.0
	Formyl leucine[1]	136.8	20	81.5	35.3
	Average				35.0
H + NH_2	Methylamine[14]	41.6	..	16.3	25.3
	Propylamine[15]	71.3	..	48.9	22.4
	Butylamine[16]	88.4	..	65.2	23.2
	Amylamine[16]	107.8	..	81.5	26.3
	Glycyl amide	60.3	20	16.3	24.0
	Leucyl amide	123.8	20	81.5	22.3
	Urea[1,17]	44.3	20	..	24.3
	Average				24.0
H + H	Formamide[18]	38.0	20	..	18.0
	Acetamide[18]	55.0	20	16.3	18.7
	Propionamide[18]	71.0	20	32.6	18.4
	n-Butyramide[18]	87.0	20	48.9	18.1
	Average				18.3
NH_2 + COOH	Hydantoic acid	77.6	20	16.3	41.3
	Calculated from terminal group volumes (35 + 24 − 18.3)				40.7

[a] Where no reference is given measurements are from this Laboratory at concentrations not greater than 0.25 m. and have not previously been reported. They were obtained at 25°.

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[9] Adam, "The Physics and Chemistry of Surfaces," Clarendon Press, Oxford, 1930.

[10] Gane and Ingold, *J. Chem. Soc.*, 2153 (1931), have derived the equation: $r = 2.98 + 1.29\ N$ Å. for the distance between the charged groups in dicarboxylic acids, a relation derived from theoretical considerations of their dissociation constants.

[11] This effect is allowed for by Sugden ["The Parachor and Valency," Routledge, London, 1930], in his estimates of the parachor, in which the molal volume is corrected for internal pressure and packing effects by being multiplied by the one-fourth power of the surface tension.

[12] Drucker, *Z. physik. Chem.*, **52**, 650 (1905).

[13] Kohlrausch, *Gött. Nachr.*, **56**, 185 (1895); Kohlrausch's value has been obtained at 18°; Drucker's value at 25° is lower than that quoted by Kohlrausch.

[14] Kanitz, *Z. physik. Chem.*, **22**, 336 (1897); measurements were made at 25°.

[15] Traube, *Ann.*, **290**, 43 (1896); measurements were made at 15°.

[16] Le Blanc and Rohland, *Z. physik. Chem.*, **19**, 261 (1896).

[17] Gucker, *Chem. Rev.*, **13**, 111 (1933).

[18] Dunstan and Mussell, *J. Chem. Soc.*, **97**, 1935 (1910).

Apparent Volume of the Amide Groups.—If the small apparent volumes of the amino acids result from their zwitterionic nature, its destruction should yield molecules resembling rather the aliphatic acids or amines than the amino acids. Formic acid combines with the amino acids with loss of a molecule of water yielding formyl compounds. Thus for a combination of formic acid and glycine we may write

$$HCOOH + NH_2CH_2COOH - H_2O = HCONHCH_2COOH$$

The formyl derivatives of the amino acids are themselves weak acids, weaker than amino acids, though stronger than unsubstituted fatty acids.[19] They possess certain of the groupings of organic acids, and certain of the groupings of peptides. All possess the CH_2 group, which we have assumed to occupy 16.3 cc. per mole. If the terminal groups of formylglycine are considered to occupy 35 cc. per mole, as in the organic acids previously considered, the volume occupied by the CONH group characteristic of the peptide or amide linkage may be estimated by the relation

$$\text{CONH} = \Phi - 16.3\ N - 35$$

The average result for the formyl compounds of the three amino acids, and for formyldiglycine, which contains two amide groups, is found to be 20.1, a value in excellent agreement with the volume of 20 cc. for the CONH group which may be calculated from the atomic volumes of Traube. This value has been adopted in the calculations in Table I, which indicates that the aliphatic acids and the formyl compounds of the amino acids may be considered as made up of CH_2 groups occupying 16.3 cc., the terminal groups characteristic of acids occupying 35 cc. and the CONH group occupying 20 cc. at 25°.

The volume occupied by the CONH group may also be compared with the dimensions revealed by recent physical measurements. Hendricks[7] gives the distance between carbon and nitrogen atoms as 1.44 and Hengstenberg and Lenel[8] between 1.4 and 1.5 Å. in their study upon glycine. The value 1.4 Å. yields 1.14 Å. as the distance in the direction of the chain, and therefore slightly more than 3.5 Å. as the distance between nitrogen atoms (1.26 + 2 × 1.14 = 3.54). This is consistent with the spacing revealed directly by the x-ray study of peptides and proteins.[20] If the length of the amide group be taken as 2.34 Å., we may estimate its cross section by means of the relation

$$V_{\text{CONH}} = 20\text{ cc.} = 2.34 \times \pi r^2 N = 2.34 \times 14.1\ N$$

On this basis the average diameter in the neighborhood of the atoms involved in peptide linkage is 4.24 Å. In a recent study on protein monolayers Hughes and Rideal state that 4 Å. "is the lesser dimension as determined by means of the x-rays of the cross section of a simple polypeptide chain" (Ref. 20b, p. 62), and Astbury[21] gives 4.5 to 5 Å. as the distance separating peptide chains in proteins.

Apparent Volume of the Terminal Groups of Aliphatic Amines, Amino Acid Amides and Urea.—The measurements previously reported upon the aliphatic amines are less satisfactory than those upon aliphatic acids, since they were made at various temperatures. They are, none the less, included in Table I.

Precisely as formic acid combines with the amino group of amino acids, yielding the amide grouping, so can the carboxylic group be combined, yielding amino acid amides. Precisely as neutralization of the amino group by formic acid renders the formyl compounds feebly acidic, so neutralization of the carboxylic group renders the molecules feebly basic.

The apparent molal volumes of the amides may be considered as the sum of the volumes of CH_2 groups, of the CONH group, and of terminal H and NH_2 groups. The value of the latter calculated in Table I is very close to that deduced from the aliphatic amines.

Just as ammonia is the smallest of the aliphatic amines, so urea may be considered the smallest of the amino acid amides. The formula of urea differs from that of glycyl amide by a CH_2 group. Subtracting 16.3 cc. from the apparent molal volume of glycyl amide yields 44.0. The apparent molal volume of urea is 44.3 cc. per mole. Subtracting 20 cc. for the amide grouping, we again obtain an estimate for the H + NH_2 grouping, which is in good agreement with that derived

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[19] The apparent molal volumes of the three formyl derivatives of amino acids thus far studied are in 80% alcohol 72.4, 105.9 and 143.7, respectively. That is to say, their apparent molal volumes increase in alcohol–water mixtures, whereas the apparent molal volumes of the zwitterionic amino acids decrease, due to increased electrostatic forces. The apparent molal volume of α-aminobutyric acid is 72.2 in 60% alcohol as compared with 76.5 cc. per mole in water. Thus we have another difference in the behavior of charged and uncharged molecules.

[20] (a) Meyer and Mark, "Der Aufbau der hochpolymeren organischen Naturstoffe," Akademische Verlagsgesellschaft, Leipzig, 1930; (b) Hughes and Rideal, *Proc. Roy. Soc.* (London), **A137**, 62 (1932).

[21] Astbury, *Trans. Faraday Soc.*, **29**, 193 (1933).

from the aliphatic amines or from glycyl or leucyl amide (Table I).

The various formulas that have been suggested for urea need not be considered here. Hendricks states that "in the crystalline state the formula must be a symmetrical one" as a result of x-ray diffraction studies (Ref. 7, p. 448). Recently, however, the theory has been advanced, partly because urea increases the dielectric constant of water, that it is to be regarded as a zwitterion.[22] This, however, has been opposed[23] upon chemical grounds. In terms of the volumes deduced, that occupied by the terminal $H + NH_2$ groups in urea occupies a volume identical with that in aliphatic amines and amino acid amides. Urea, then, shows no electrostriction of solvent not characteristic of these molecules. The increase in the dielectric constant of water produced by urea would therefore appear to be due to the polarity of the carbonyl and amino groups of the molecule, rather than to its charged condition.

Apparent Volumes of the Terminal Groups of Aliphatic Amides.—Hydrogen atoms may be considered as terminal groups of the amides of aliphatic acids. The first member of the series, formamide, contains no CH_2 group. Its apparent molal volume may be taken as 38 cc. Subtracting 20 cc. for the amide linkage, we obtain an estimate of 18 cc. per mole for the apparent volume ascribed to the terminal hydrogen atoms. Comparable estimates have been made from the molal volumes of other aliphatic amides, which have been studied by Dunstan and Mussell.[18] The average of the differences in the last column of Table I, 18.3 cc. per mole, yields an estimate of the space occupied by the terminal hydrogens and, of course, of intermolecular space.

This value suggests that the carbonyl group in the amide linkage occupies far more space than the NH group. Subtracting 18.3 cc. for the hydrogens and 20 cc. for the amide group from the molal volume of urea, leaves 6.0 cc. per mole for the NH and, therefore, 14 cc. per mole for the carbonyl group. Traube's estimates for these groups are 4.6 and 15.4 cc. Neither estimate is readily interpretable from x-ray diffraction studies upon urea or other related substances. These indicate that the nitrogen atom is only slightly smaller than the carbon atom, whereas the volumes occupied by these respective atoms according to Traube are 9.9 and 1.5 cc. per mole, respectively. There remains no doubt, therefore, that the type of analysis upon molecular volumes that Traube employed, and that has here been followed, agrees with the evidence derived from x-ray studies as far as the groupings within the molecules are concerned, but leads to different conclusions if we attempt to derive the volumes of individual atoms from those of terminal groups. Subtracting Traube's atomic volumes from the volumes deduced for the terminal groups considered, leaves for the amide series 12.1, for the acid series 13.0, for the amine series 13.2 and for hydantoic acid 14.1 cc. per mole. A proportional correction for the temperature difference between 15 and 25° does not appreciably diminish the difference between these values, which may be compared with the so-called covolumes of Traube. The apparent volumes calculated for terminal groups thus largely reflect intermolecular forces.

Apparent Volume of the Terminal Groups of Amino Acids.—Hydantoic acid may be considered to be a peptide of carbamic acid and glycine, but it appears not to be a zwitterion.[24] The terminal groups at the ends of its molecules are, respectively, a carboxyl and an amino group. The apparent volume occupied by them, 41.3 cc., may be calculated by subtracting from the apparent molal volume of hydantoic acid the values we have assumed for the CH_2 and CONH groups.

A quite different calculation also yields an estimate of the volume of NH_2 and COOH considered as terminal groups. The sum of the volumes of the terminal groups characteristic, respectively, of acids and amines, may be diminished by that characteristic of the hydrogen atoms considered as terminal groups for the aliphatic amides:

$$\underbrace{\mathrm{H + NH_2}}_{24} \underset{+}{+} \underbrace{\mathrm{H + COOH}}_{35} \underset{-\,18.3}{-\,2\mathrm{H}} \underset{=}{=} \underbrace{\mathrm{NH_2 + COOH}}_{40.7}$$

The agreement is excellent. It indicates that the electrical properties of hydantoic acid do not differ from those of aliphatic acids or amines or the formyl compounds or the amides of the amino acids. Since none of these compounds are considered to be highly dissociated, the conclusion appears inevitable that hydantoic acid does not produce marked electrostriction of the solvent.

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(22) Devoto, *Gazz. chim. ital.*, **60**, 520 (1930); **61**, 897 (1931).

(23) Ebert, *Z. physik. Chem.*, **121**, 385 (1926).

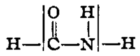
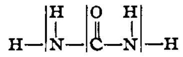
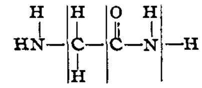
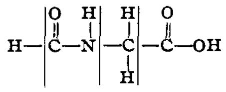
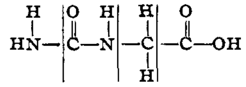
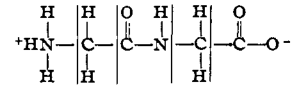
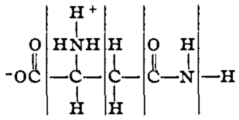
(24) Devoto, *Gazz. chim. ital.*, **63**, 50 (1933), has reported that hydantoic acid increases the dielectric constant of water as much as a β-amino acid; a result not readily reconciled with its apparent molal volume.

Hydantoic acid differs from formylglycine by the replacement of a terminal hydrogen atom by an amino group. The basicity of this amino group appears to be[25] so diminished by the neighboring strongly electronegative carbonyl group that the molecule is feebly acidic, thus resembling the fatty acids rather than the zwitterionic amino acids.

II. **Apparent Molal Volumes of the Aliphatic Amino Acids.**—Hydantoic acid differs from glycylglycine by one CH_2 group. These relations are indicated in the accompanying table.

TABLE II

APPARENT MOLAL VOLUMES OF SUBSTANCES CONTAINING THE AMIDE LINKAGE, BUT DIFFERENT TERMINAL GROUPS

Substance	Structure	App. molal vol. cc. per mole	Nature of the terminal group
Formamide	 $H-\overset{\overset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-H$	38.0	$H+H$
Urea	 $H-\overset{\overset{H}{|}}{N}-\overset{\overset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-H$	44.3	$H+NH_2$
Glycylamide	 $\overset{\overset{H}{|}}{HN}-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-H$	60.3	$H+NH_2$
Formylglycine	 $H-\overset{\overset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{O}{\|}}{C}-OH$	70.6	$H+COOH$
Hydantoic acid	 $\overset{\overset{H}{|}}{HN}-\overset{\overset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{O}{\|}}{C}-OH$	77.6	NH_2+ $COOH$
Glycylglycine	 $^{+}\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{HN}}-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{O}{\|}}{C}-O^{-}$	77.2	$-NH_3^++$ COO^-
Asparagine	 $^{-}O\overset{\overset{O}{\|}}{C}-\underset{\underset{H}{|}}{\overset{\overset{\overset{H^+}{|}}{HNH}}{C}}-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{O}{\|}}{C}-\overset{\overset{H}{|}}{N}-H$	78.0	$-NH_3^++$ COO^-

Glycylglycine and asparagine, which are isomeric compounds, have apparent molal volumes of 77.2 and 78.0 cc. per mole, respectively. Both are zwitterions, and the somewhat larger molecular volume of asparagine may be ascribed to the closer proximity of its $—NH_3^+$ group to the $—COO^-$ group.

Hydantoic acid contains one less CH_2 group than asparagine or glycylglycine. Its molal volume might, therefore, be expected to be diminished by 16.3 cc. per mole. It is, however, intermediate between that of asparagine and glycylglycine. The CH_2 group of the latter may be considered as protecting the amino group or rather the charged ammonium group from the carbonyl group, whereas the amino group of hydantoic acid resembles that of urea[27] rather than of the peptides.

The comparison between hydantoic acid and glycylglycine yields an estimate of the electrostriction of solvent molecules produced by the charged COO^- and $—NH_3^+$ groups, at the concentrations studied. This difference may be considered very accurately known since it depends only upon the volume of the CH_2 group, the best known element of volume in the systems that have been analyzed.

The comparison that has been made of the molal volumes of uncharged substances containing the same chemical groups renders it probable that these occupy the same space in molecules of quite widely different nature. It may be assumed that the apparent molal volumes of the amino acids could also be calculated in terms of the deduced elements of volume, were it not for the electrostriction of the solvent due to the positive and negative charges of their neutral molecules. The increment in volume due to each CH_2 and CONH group appears to be the same as in the other compounds considered. The difference between these and the amino acids inheres in the value ascribed to the terminal ammonium and carboxyl groups. If it be assumed that these occupy the same volume as the uncharged amino and carboxyl groups—that is, that the movement of a proton from the latter to the nitrogen results in no change in volume—then the difference between the observed apparent molal volumes and those calculated from the volumes of constituent groups reveals electrostriction of the solvent. The calculations in Table III have been made on this basis.

Since Traube's estimate of the CH_2 group is identical with that employed in all the calculations, and since it has been shown that his system of atomic volumes also yields an estimate identical with that observed for the apparent molal

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[25] Proximity to a COO^- or $C{=}O$ group diminishes basic strength as the following data indicate

	pK'		pK'
Isoamylamine	10.70	Glycine	9.72
δ-Aminovaleric acid	10.69	Asparagine	8.87
γ-Aminovaleric acid	10.40	Glycylglycine	8.07
α-Aminovaleric acid	9.72	Glycylglycylglycine	7.91

The value of pK' for acetamide is approximately 1.7 [Euler and Olander, *Z. physik. Chem.*, **131**, 107 (1927)]. Here as in hydantoic acid the carbonyl group immediately adjoins the amino group. For a further discussion of these data and of their sources see Ref. 26, p. 842–845.

[26] Cohn, *Ergebn. d. Physiol.*, **33**, 781 (1931).

[27] The amino acid amides are also stronger bases than urea because of the protective action of the intervening CH_2 group against the strongly electronegative carbonyl group.

TABLE III

INFLUENCE OF DISTANCE SEPARATING THE CHARGED GROUPS OF AMINO ACIDS AND PEPTIDES UPON ELECTROSTRICTION OF THE SOLVENT

Concentration 0.25 *m*, temperature 25°

Substance	Volume occupied by groups CH_2	other groups	terminal NH_3 + COOH	Apparent molal volume Calcd.	Obs.	Estimated electrostriction per mole
Glycine	16.3		40.7	57.0	43.5	13.5
α-Alanine	32.6		40.7	73.3	60.6	12.7
Serine	32.6	(—O— = 0.4)	40.7	73.7	60.8	12.9
α-Aminobutyric acid	48.9		40.7	89.6	76.5	13.1
α-Aminoisobutyric acid					78.1	11.5
α-Aminovaleric acid	65.2		40.7	105.9	92.7	13.2
α-Aminoisovaleric acid					91.3	14.6
α-Aminocaproic acid[a]	81.5		40.7	122.2	108.4	13.8
α-Aminoisocaproic acid[a]					107.5	14.7
					Average	13.3
β-Alanine	32.6		40.7	73.3	58.9	14.4
β-Aminobutyric acid[b]	48.9		40.7	89.6	76.4	13.2
γ-Aminovaleric acid	65.2		40.7	105.9	90.0	15.9
ε-Aminocaproic acid	81.5		40.7	122.2	104.9	17.3
Lysine[c]	81.5	(NH = 4.6)	40.7	126.8	108.5	18.3
Diglycine	32.6	(CONH = 20)	40.7	93.3	77.2	16.1
Triglycine	48.9	(2CONH = 40)	40.7	129.6	113.5	16.1

[a] The small solubility of these amino acids made it necessary to study them at lower concentrations; namely, leucine at 0.168, and norleucine at 0.084. [b] β-Aminobutyric acid was studied at 0.5 *m*. [c] Lysine is an ε-amino acid in the pure state.[26]

volume of the first member of the amino acid series, glycine, it follows that his system would also hold for the other α-amino acids.[1] The agreement suggests that that part of the volume ascribed to terminal groups, which is concerned with intermolecular space (termed by Traube the co-volume) is in the case of α-amino acids compensated by the increased density of the solvent due to electrostriction. The electrostrictive effect due to the positively and negatively charged groups of α-amino acids is far smaller, however, than it is if these are at a greater distance from each other. Instead of being approximately 13.3 cc. per mole as in α-amino acids, it appears to be approximately 18 cc. per mole when the charged ammonium group is in the ε position.

III. Apparent Molal Volumes of Cyclic Amino Acids.—Cyclic amino acids are also to be regarded as zwitterions. In order to estimate the electrostriction due to their charged groups it is necessary to compare their apparent molal volumes with those of comparable uncharged molecules. When an hydantoic acid is heated in acid solution ring formation with loss of a molecule of water follows. The resulting hydantoin, of which three have been prepared and studied, may be considered as constituted of two amide linkages and one or more CH_2 groups. Apparent molal volumes calculated in this manner are always smaller than the observed apparent

TABLE IV

INFLUENCE OF THE CHARGED GROUPS OF CYCLIC AMINO ACIDS UPON ELECTROSTRICTION OF THE SOLVENT

Substance	Apparent molal volume Calcd.	Obs.	Difference	Estimated electrostriction per mole
Nitrogen containing rings				
Pyridine[15a]	66.5	76.7	+10.2	
Piperazine[15]	73.6	80.7	+ 7.1	
Piperidine[15]	85.1	94.9	+ 9.8	
Hydantoin	56.3	65.2	+ 8.9	
Hydantoin of aminobutyric acid	88.9	99.1	+10.2	
Hydantoin of leucine	121.5	131.5	+10.0	
		Av.	+ 9.4	
Proline	85.4	81.0	− 4.4	13.8
Hydroxyproline	87.7	84.4	− 3.3	12.7
Histidine	97.9	99.3	− 1.4	10.8
Benzene rings				
Phenol[15a]	80.3	84.0	+ 3.7	
Hydroquinone[16]	82.6	87.0	+ 4.4	
Phlorglucine[15]	84.9	89.1	+ 4.2	
Cresol[15]	96.4	100.7	+ 4.3	
		Av.	+ 4.2	
Phenylalanine	130.8	121.3	− 9.5	13.7
Tyrosine	133.1			
Tryptophane	155.0	144.1	−10.9	15.1
Meta aminobenzoic acid[15a]	98.4	90.3	− 8.1	12.3
Ortho aminobenzoic acid[15]	98.4	96.7	− 1.7	5.9
Para aminobenzoic acid[15]	98.4	97.3	− 1.1	5.3

[a] Measurements by Traube were made at 15°; our measurements at 25°.

molal volumes. The difference cannot here be ascribed to terminal groups. If ascribed to intermolecular space the estimate is smaller by something over 2 cc. than that derived from the amide series, and something over 3 cc. than that derived from the acid or amine series (p. 787). Traube long since noted this phenomenon not only for the pyridine and piperidine, but also for other nitrogenous rings, as the pyrrole, pyrrolidine and pyrazole rings.[6] Some of his observations are recorded in Table IV.

Proline may be considered as the anhydride of δ-aminovaleric acid. Its observed apparent molal volume, and that of hydroxyproline, are smaller than calculated apparent molal volumes. Comparison with the uncharged ring compounds yields estimates for electrostriction comparable to that produced by aliphatic α-amino acids. The estimate made in this way for histidine, which contains the imidazole ring, is somewhat lower.

Tyrosine may be regarded as constituted of alanine and phenol. It is very insoluble and has not been studied directly. Phenylalanine, however, has been measured. Its apparent molal volume is appreciably smaller,[28] whereas those of phenol and other uncharged ring compounds are greater than calculated. Tryptophane may be considered as constituted of alanine and indole. The difference due to this double ring may be somewhat greater, and account for the slightly greater estimated electrostriction. These results again demonstrate that the cyclic amino acids are to be regarded as zwitterions.

The aminobenzoic acids, in which the amino group is directly attached to the benzene ring, do not, however, exist overwhelmingly as zwitterions in aqueous solution. Bjerrum[29] and Ebert[23] estimated from dissociation constants that the ratio of zwitterions to uncharged molecules is not far from unity for the aminobenzoic acids.[30] Michaelis and Mizutani,[31] from electromotive force measurements in alcohol–water mixtures, concluded that the uncharged molecules predominate, and Birch and Harris[32] reached a similar conclusion regarding para aminobenzoic acid from its dissociation constants in the presence of formaldehyde. Hedestrand[33] reported that the aminobenzoic acids—in pronounced contrast to the aliphatic amino acids—lower the dielectric constant of water and inferred that the uncharged molecule is the predominant form, but Devoto[34] has found that meta aminobenzoic acid increases the dielectric constant of water by 41 units per mole, while the ortho and para acids have but slight influence on the dielectric constant. Solubility studies[35] also show the meta acid to be more soluble in water, and much less soluble in organic solvents than the ortho and para acids.

Traube has measured the apparent molal volumes of the aminobenzoic acids and of their sodium salts.[15] The volumes of the sodium salts are all very nearly identical (o = 89.2, m = 89.2, p = 88.1 cc. per mole), as might be expected since they are all ionized to about the same extent. The isoelectric acids, however, differ markedly from one another, the apparent volume of the meta acid being much smaller than that of the ortho or para acid.

The apparent volumes of the sodium salts of glycine, alanine and valine are approximately the same as those of the isoelectric amino acids (see Table V). If the aminobenzoic acids existed exclusively as zwitterions, we might expect the same to be true of them. The volume of *m*-aminobenzoic acid is indeed of this order, suggesting without further calculation a high zwitterionic ratio.

Both *o* and *p*-aminobenzoic acids clearly contain a smaller but not a negligible zwitterionic ratio. The amount of electrostriction due to each is estimated in Table IV. This calculation suggests a new method of evaluating the zwitterionic ratio, in good agreement with evidence from several other sources.

Traube recognized the anomalous behavior of the aminobenzoic acids and also of glycine, and attempted to explain it in terms of ring formation between the amino and carboxyl groups. Plausible as this hypothesis was at the time, it has been shown by Pfeiffer[36] to be untenable on stereochemical grounds, and the observed phenomena are readily interpretable in terms of the electrostriction hypothesis.

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(28) Traube noted the smaller difference from atomic volumes of substances containing the benzene and hexamethylene rings.[6] We have preferred not employing the so-called covolume of Traube, but rather comparing comparable charged and uncharged compounds.

(29) Bjerrum, *Z. physik. Chem.*, **104,** 147 (1923).

(30) There is a misprint in Ebert's table. The correct values for this ratio from dissociation constants are approximately 0.22, 2.3 and 0.15, respectively, for ortho, meta and para benzoic acids.

(31) Michaelis and Mizutani, *Z. physik. Chem.*, **116,** 135 (1925).

(32) Birch and Ha.ris, *Biochem. J.*, **24,** 1080 (1930).

(33) Hedestrand, *Z. physik. Chem.*, **135,** 36 (1928).

(34) Devoto, *Gazz. chim. ital.*, **63,** 247 (1933).

(35) (a) Edsall and Blanchard, THIS JOURNAL, **55,** 2337 (1933); (b) de Coninck, *Ann. chim. phys.*, [7] **4,** 528 (1895).

(36) Pfeiffer, *Ber.*, **55,** 1762 (1922).

IV. Apparent Molal Volumes of Amino Acid Salts.—The salts of the amino acids are generally considered completely dissociated. The resulting ions produce electrostriction of the solvent, and the apparent molal volumes observed are therefore appreciably smaller than would be those of comparable uncharged molecules. Whether or not they are smaller than the apparent molal volumes of the zwitterions depends upon the nature and apparent volume of the inorganic ion of the amino acid salt. The apparent molal volumes of certain of the salts of amino acids are reported in Table V. The sodium salts of α-amino acids appear to occupy volumes extraordinarily close to those of the free acids. The apparent volumes of the other salts studied are appreciably larger. Those of lithium salts are, however, presumably smaller.

TABLE V

APPARENT MOLECULAR VOLUMES OF AMINO ACID SALTS

Concentration 0.25 *m*, temperature 25°

Amino acid	Zwitterion Φ	Sodium salt Φ	Potassium salt Φ	Hydrochloride Φ	Hydrobromide Φ
Glycine	43.5	44.4	54.2	68.3	75.3
Alanine	60.6	60.0	70.3	86.1	93.2
Valine	91.3	89.6	99.6	117.6	124.5
Aspartic acid[a]		65.6	75.9	99.3	106.2

[a] Only the mono-sodium and potassium salts are given in this table. The apparent molal volumes of the di-sodium and di-potassium salts are 62.3 and 83.1 cc. per mole, respectively.

Aspartic acid, like certain of the other amino acids and peptides, is very insoluble in water, rendering difficult accurate measurements of its apparent molal volume. The acid and alkaline salts are more soluble. Estimation of the relations between the apparent volumes of the amino acid salts and of a free amino acid, when all are readily measurable, should render it possible to estimate the apparent molal volumes of amino acids which are insoluble in the free state.

If from the sum of the apparent molal volumes of the sodium salts, and of the hydrochlorides, of an amino acid is subtracted the apparent molal volume of sodium chloride, the result should yield the sum of the apparent molal volumes of the amino acid anion and cation. This method of calculation assumes only the additive nature of molal volumes. It has been carried out in Table VI, on the basis of the results in Table V, for all the combinations studied. The apparent molal volumes of the inorganic salts, at the same concentration and temperature, are recorded in parentheses in the table. Their subtraction from those of the amino acid salts taken in pairs, yields estimates which are in excellent agreement with each other.

The electrostriction due to the charged groups of amino acids, when they are situated on different molecules, may also be calculated from these results. Assuming the molal volume of each amino acid ion to be equal to the sum of the apparent molal volume of the zwitterion and the electrostriction produced—previously calculated to be 13.3 cc. per mole for α-amino acids—results in estimates of electrostriction for anion plus cation of 18.6 cc. for glycine, 19.1 cc. for alanine and 19.7 cc. for valine.[37] The magnitude of this effect would appear to increase with increase in the hydrocarbon chain. This drift may reflect the change of electrostriction with concentration of these substances,[38] or more deep-seated structural forces.

Estimation from these results of the apparent molal volume of either anion or cation involves knowledge of the apparent molal volumes of inorganic ions. The assumption of a value for the apparent molal volume of any ion would fix that of all the other inorganic ions and also of the amino acid anions and cations. No assumption is involved in the estimation of the apparent molal volume of amino acid ions other than those involved in the estimation of the ion of an inorganic salt. The further calculations in Table VI have been based tentatively upon the estimates of the individual ions due to Webb.[39] These have been corrected from infinite dilution to

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(37) An analysis of Weber's (Ref. 4) measurements of the volume changes on neutralization of acids, bases and amino acids, yields values for electrostriction of the same order of magnitude. The volume change due to the dissociation of acetic, propionic and butyric acids yields

$CH_3COOH = CH_3COO^- + H^+ \qquad \Delta V = -10.3$ cc.
$C_2H_5COOH = C_2H_5COO^- + H^+ \qquad \Delta V = -12.6$ cc.
$C_3H_7COOH = C_3H_7COO^- + H^+ \qquad \Delta V = -13.1$ cc.

and for methyl and ethyl amine and glycine ethyl ester

$CH_3NH_2 + H^+ = CH_3NH_3^+ \qquad \Delta V = -5.5$ cc.
$C_2H_5NH_2 + H^+ = C_2H_5NH_3^+ \qquad \Delta V = -3.6$ cc.
$C_2H_5OOCCH_2NH_2 + H^+ = C_2H_5OOCCH_2NH_3^+ \qquad \Delta V = -5.8$ cc.

On adding the volume changes for the two types of reaction, the electrostriction produced by anion and cation

$$RCOOH + RNH_2 = RCOO^- + RNH_3^+$$

appears to be, as a maximum, 18.9 cc. per mole.

(38) We have since determined [Cohn, *Science*, **79**, 83 (1934)] that the rule: $\Phi = \Phi_0 + K\sqrt{C}$ holds for glycine and its salts, though not for large amino acids. For glycine Φ_0 is 42.8, for its sodium salt 42.4 and for its hydrochloride 67.0. At infinite dilution the calculation comparable to that in Table VI yields for the partial molal volumes of anion plus cation: (42.4 + 67.0 − 15.8 = 93.6) and for the electrostriction 20.0 cc. for $—NH_3^+ + —COO^-$ at infinite distance and dilution.

(39) Webb, THIS JOURNAL, **48**, 2589 (1926).

TABLE VI

APPARENT MOLAL VOLUMES OF AMINO ACID ANIONS AND CATIONS

Concentration 0.25 *m*, temperature 25°

		Glycine	Alanine	Valine	Aspartic acid	
Apparent molal volumes of anion and cation: $A^+ + A^-$						
$Na^+A^- + AH^+Cl^- - Na^+Cl^-$	(17.6)	95.1	128.5	189.6	147.3	
$Na^+A^- + AH^+Br^- - Na^+Br^-$	(24.5)	95.2	128.7	189.6	147.3	
$K^+A^- + AH^+Cl^- - K^+Cl^-$	(27.8)	94.7	128.6	189.4	147.4	
$K^+A^- + AH^+Br^- - K^+Br^-$	(34.7)	94.8	128.8	189.4	147.4	
$2(^+A^- + 13.3) - 19.0$		94.6	128.8	190.2	. . .	
Apparent molal volume of anion:				A^-	$^+A^=$	$A^=$
$Na^+A^- - Na^+$	(−3.3)	47.7	63.3	92.9	68.9	68.9
$K^+A^- - K^+$	(6.9)	47.3	63.4	92.7	69.0	69.3
Apparent molal volume of cation: A^+						
$AH^+Cl^- - Cl^-$	(20.9)	47.4	65.2	96.7	78.4	
$AH^+Br^- - Br^-$	(27.8)	47.5	65.4	96.7	78.4	

the concentration studied by proportionately diminishing the estimated electrostriction of the ions, and are given in parentheses. Their adoption does not permanently commit us to Webb's theory, or to the above method of correction for the effect of concentration, for calculations comparable to those given in the table could be carried out with any other values subsequently proposed for the apparent molal volumes of ions, so chosen that their sum yielded those of the salts.

The apparent molal volumes of the glycine anion and cation estimated in this way are identical. That is to say, the electrostriction due to each is 9.3 cc. per mole.[40] This distribution of the total electrostriction between the amino acid ions is, of course, dependent upon the values assigned to the inorganic ions. The same values for the latter, however, lead to quite different estimates for the electrostriction due to anion and cation in the case of the larger amino acids studied. Thus a calculation comparable to that upon glycine indicates that the electrostriction due to the anion of alanine is 10.5, and of valine 11.8 cc., whereas that due to the cation of alanine is 8.6 and of valine 7.9 cc. per mole. Whether these drifts reflect structural forces, or are dependent upon the influence of the molal volume upon the change in electrostriction with concentration, remains to be investigated.

The apparent molal volumes of both amino acid anions and cations are greater than those of the zwitterions by from 1.5 to 6 cc. per mole. The smaller apparent molal volumes of zwitterions than ions presumably account, in part, for the minimum in viscosity of such substances in the neighborhood of their isoelectric points. The larger number of charges near the isoelectric point accounts for the greater electrostriction and the smaller apparent volume. It should be pointed out, however, that in the case of amino acids, peptides or proteins, with an unsymmetrical number of charges, the minimum apparent molal volume and the maximum electrostriction should coincide not with the isoelectric point, but with the point of maximum charge (Ref. 26, p. 832). In the case of aspartic acid this would be characteristic of the ion bearing two negative and one positive charges, into which the acid salt dissociates. Although the apparent molal volumes of the monovalent anions of the other amino acids are larger than those of the zwitterions, the ion into which the mono-sodium and potassium salts of aspartic acid dissociate is smaller by approximately the same amount. This observation might indeed be put forward, were further evidence needed, in favor of the view that the condition of maximal charge does not necessarily coincide with the isoelectric point.

The apparent molal volume of this trivalent ion cannot, therefore, be employed in calculations such as apply to monovalent ions. The monovalent cation of aspartic acid might, however, be employed in estimating the value of the zwitterion assuming the electrostriction due to the cation to be approximately nine cc. per mole, by means of the equation

$$^+A^- + 13.3 - 9.0 = 78.4$$

The result that $^+A^-$ is 74.1 cc. per mole may be compared with the apparent molal volume of aspartic acid calculated by means of the atomic volumes of Traube, namely, 74.6 cc. per mole.[41] This excellent agreement between estimates of the apparent molal volume of aspartic acid made on the basis of Traube's atomic volumes, and of the study of its soluble salts, tends to confirm the validity of calculations of the type introduced, and demonstrates the dependence of the apparent molal volumes of amino acid ions and zwitterions upon the influence of the number and distribution of the charges borne by these molecules upon the electrostriction of the solvent.

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[40] At infinite dilution the electrostriction due to the anion is 9.9 and to the cation 10.1 cc. per mole.

[41] Dalton and Schmidt [*J. Biol. Chem.*, **103**, 549 (1933)] have recently reported a value of 75.2 for the apparent volume of *dl*-aspartic acid at 25°. Their estimates for other amino acids essentially confirm ours.

The modern theory of electrostriction[39,42] relates its magnitude to the radii of the ions producing it. The smaller the ion, the more intense the electric field surrounding it, and the greater the electrostriction. Under the term electrostriction we have combined all forces leading to the increased density of solutions. Moreover, the charged groups with which we are concerned cannot, it is true, attract solvent molecules in all directions, because they are attached to the hydrocarbon chain. An attempt to calculate the diminution of electrostriction resulting from this interference involves arbitrary assumptions.

The electrostrictions tentatively estimated for amino acid anions range upward from 9.4 to 12.0 cc., whereas those due to cations range downward to 7.9 cc. per mole. The largest and smallest of these are of the order that Webb[39] calculates for spherical ions with radii of exclusion, respectively, of 1.7 and 2.25 Å., and that Vosburgh, Connell and Butler[43] calculate for ions with radii of 2.35 and 2.8 Å.

These dimensions are not dissimilar to those of the terminal groups we have considered.

Terminal groups.......	$H + NH_2$	$H + COOH$	$NH_2 + COOH$
Radii from sum of atomic volumes, Å.	1.62	2.04	2.19
Radii from volumes of terminal groups, Å.	2.12	2.40	2.52

The amount of electrostriction due to the various amino acids varies far less than their volumes or dimensions. The greatest uncertainty in estimating the dimensions of amino acids and peptides inheres in the dimensions ascribed to the terminal groups, and becomes smaller the larger the molecule. On the assumption that glycine is a sphere an estimate that it has a cross section of 20.9 sq. Å. may be made from its apparent molal volume. Provided the latter be corrected for electrostriction the cross section becomes 25 sq. Å. Adam's estimate of the cross section of aliphatic acids in dilute HCl is 25.1 sq. Å. (Ref. 9, p. 50). The radii in Ångström units of the amino acids considered as spheres are

Number of CH_2 groups.......		1	2	3	4	5
Radii of spheres estimated from apparent molal volumes	r	2.58	2.88	3.12	3.30	3.49
Radii of spheres estimated from volumes, corrected for electrostriction.............	r	2.82	3.08	3.29	2.46	3.63
Radii and lengths of cylinders estimated from volumes of α-amino acids, corrected for	r	2.90	2.83	2.78	2.75	2.73
electrostriction	l	3.56	4.82	6.08	7.34	8.60
Length of cylinders of radius 2.61 estimated from volumes of terminal amino acids, corrected for electrostriction.	l	4.41	5.67	6.93	8.19	9.45

These estimates are satisfactory for amino acids with branched chains.[44]

The larger normal amino acids and the peptides cannot be considered spherical. They can perhaps more simply be considered as cylinders,[45] having the cross section and lengths, respectively, of the CH_2, CONH and terminal groups. In α-amino acids other than glycine, the length of terminal groups in the direction of the hydrocarbon chain can scarcely be greater than 2.3 Å., but the cross section through the carbon atom bearing the amino group will be greater than other segments. When the amino group is terminal, the average radius approaches that of the CH_2 groups as lower limit, yields an estimate of 3.15 Å.[46] for the length of terminal groups, and permits such amino acids to be considered as cylinders of constant radius. On this basis di- and triglycine have average radii of 2.48 and 2.43 and lengths of 8.0 and 11.5 Å. These approximate calculations suffice to indicate that the charges of these ions and zwitterions, as contrasted to those of inorganic ions, cannot be considered as distributed over their molecules, but rather as limited to the regions surrounding the charged groups.

Summary

1. The positive and negative charges borne by isoelectric amino acids result in electrostriction of the solvent.

2. The apparent molal volumes of the amino acids and peptides have been determined and analyzed in terms of the volumes occupied by the internal CH_2 and CONH groups, and of the amino and carboxyl groups. The dimensions of the former are identical with those of the same groups in the liquid state, or in uncharged molecules, and are considered in terms of the thickness of surface layers and of x-ray diffraction data.

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(42) (a) Zwicky, *Physik. Z.*, **27**, 271 (1926); (b) Evjen and Zwicky, *ibid.*, **33**, 860 (1929).

(43) Vosburgh, Connell and Butler, *J. Chem. Soc.*, 933 (1933).

(44) The radius of a branched chain considered as a cylindrical segment is approximately 3.7 Å.

(45) Meyer and Mark (Ref. 20) have employed the equation for the cylinder in estimating the molal volumes of aliphatic hydrocarbons.

(46) The sum of the interatomic distances in the direction of the chain should from x-ray and band spectrum data be approximately 3.1 Å. The length of a segment can, therefore, scarcely be shorter.

3. The smaller apparent molal volumes occupied by terminal groups in the amino acids being ascribed to electrostriction of solvent molecules, the apparent volumes of the uncharged amino and carboxyl groups have been estimated from the molal volumes of aliphatic acids, amides and amines and of hydantoic acid.

4. Apparent molal volumes yield a criterion for distinguishing between zwitterions and uncharged molecules. The measurements considered indicate that urea and hydantoic acid are not zwitterions, and that the proportion of the molecules of *m*-aminobenzoic acid that are zwitterions, is far greater than of the other aminobenzoic acids.

5. Separation of the charged groups from each other in a zwitterion increases electrostriction, which amounts to 13.3 cc. per mole when the charged amino group is in the α position and approximately 18 cc. per mole when in the ϵ position.

6. The apparent molal volumes of amino acid salts have been analyzed in terms of the volumes and electrostrictions of their constituent ions. The electrostriction due to amino acid ions appears to be slightly greater than that of the same charged groups of zwitterions even when the charged groups are separated by five carbon atoms.

7. The electrostrictions suggest the approximate dimensions of the charged groups, and the molal volumes the dimensions of amino acid and peptide molecules.

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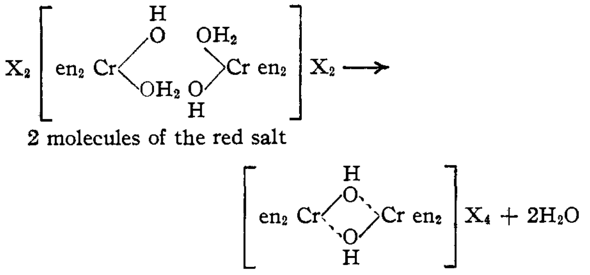
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

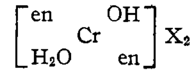
The Nature of Chromium Oxychloride Hydrosols

BY ARTHUR W. THOMAS AND FREDERICK C. VON WICKLEN

The possibility of one coördinative bond of each of two metal atoms being shared by one hydroxyl (or hydroxo) group was first suggested by Pfeiffer.[1] To compounds containing such groups Werner[2] gave the name, "ol-compounds" and described the preparation of octammino-di-ol-dicobalti sulfate from hydroxo-aquo-tetrammino-cobalti sulfate. Then Pfeiffer,[3] observing that the red colored diethylenediamine-hydroxo-aquo-chromi salts were converted to crystalline blue violet salts with the loss of one molecule of water per atom of chromium upon heating to 100–120°, proposed the formation of the di-ol compound as the most satisfactory explanation, according to the scheme



and pointed out "Dass dieser Vorgang manche Analogie mit der Polymerisation organischer Verbindungen, z. B. der der Aldehyde zeigt, ist ohne weiteres ersichtlich."[3a] Since the flesh colored di-ethylene-diamine-hydroxo-aquo salts did not undergo this change upon heating, he ascribed to them the *trans* configuration



and to the red salt, the *cis* structure.

Bjerrum[4] found polymerization of basic chromic salts to occur upon heating of their aqueous solutions producing increases in molecular weight to as high as 750. These products were referred to by him as "latent basic" compounds.[5]

Thus from Bjerrum's discoveries concerning the extent of polymerization of his "latent basic" compounds, one might imagine that he had in solution, among other complexes, dodecaol-dodecaaquohexachromi chloride[6] of molecular weight 732.

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[1] (1) P. Pfeiffer, *Z. anorg. Chem.*, **29**, 107 (1902).

[2] (2) A. Werner, *Ber.*, **40**, 2113, 4436 (1907).

[3] (3) P. Pfeiffer, *Z. anorg. Chem.*, **56**, 261 (1908).

[3a] (3a) "That this reaction shows many analogies to the polymerization of organic compounds, for example of the aldehydes, is quite obvious."

[4] (4) N. Bjerrum, *Z. physik. Chem.*, **59**, 336 (1907); **73**, 724 (1910); "Studier over Basike Kromiforbindelser," Kopenhagen, 1908.

[5] (5) It should be recalled that T. W. Richards and F. Bonnet, *Z. physik. Chem.*, **47**, 29 (1904), had reported the existence of a variety of basic chromic sulfate solutions containing particles of high molecular weight.

[6] (6) (a) E. Stiasny and O. Grimm, *Collegium*, **691**, 505 (1927); (b) E. Stiasny and D. Balanyi, *ibid.*, **682**, 86 (1927).