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Macromolecular chemistry

Nobel Lecture, December 11, 1953

Macromolecular chemistry is the youngest branch of organic chemistry and as such has experienced the honour of the award of the Nobel Prize for Chemistry. I sincerely hope that this great distinction will be the means whereby macromolecular chemistry will undergo further fruitful development.

Some few months after I had the opportunity of speaking in this auditorium on the development of macromolecular chemistry into a new branch of organic chemistry at the International Congress for Pure and Applied Chemistry¹, it is today my duty to describe to you the characteristic features of macromolecular chemistry and demonstrate the new features which it introduces into organic chemistry.

The macromolecular compounds include the most important substances occurring in nature such as proteins, enzymes, the nucleic acids, besides the polysaccharides such as cellulose, starch and pectins, as well as rubber, and lastly the large number of new, fully synthetic plastics and artificial fibres. Macromolecular chemistry is very important both for technology and for biology.

In common with all organic compounds, the structure of the organic macromolecular compounds (inorganic macromolecular compounds are not discussed in the following) involves in addition to carbon atoms, chiefly hydrogen, oxygen, and nitrogen atoms which in accordance with the laws of Kekulé's structural theory are bound by chief valences². The only difference between macromolecules and the small molecules of low molecular substances is one of structural size. If it is desired to lay down a boundary between macromolecular and low molecular compounds - there are of course transitions linking the two groups - the substances with a molecular weight greater than ten thousand, i.e. the molecules of which consist of one thousand and more atoms, may be classified as macromolecular. Beyond roughly this size, characteristic macromolecular properties occur. So far no upper limits can be given for the size of the macromolecules. Macromolecular compounds with a molecular weight of several millions are known,

i.e. compounds in which one million and more atoms form the macromolecules in the manner prescribed by Kekulé's structural theory.

In recent decennia the field of macromolecular chemistry has been the scene of very intensive scientific and technical activity. I personally have been concerned³ with macromolecular chemistry since 1920 initially at the Federal Institute of Technology in Zurich. Since my move to the chemical laboratory in Freiburg University I have devoted myself entirely to extending this field which, since my retirement, has been further studied in a special research institute in Freiburg.

In this work I have been assisted by a number of first-class colleagues who have published valuable research on this field. Here I should like to mention the oldest of them, Signer⁴, now in Bern, whose support during the discussions on the structure of these compounds in the 1920's was very valuable and who introduced the flow birefringence method for studying the particle shape of macromolecular substances. In addition Schulz, now in Mainz, extended the physico-chemical studies in the last two decennia, especially the molecular weight determination of macromolecular substances. He also worked on the kinetics involved in the formation of macromolecular substances⁶. Kern⁷, now in Mainz, studied the behaviour of polyelectrolytes. Husemann⁸, Freiburg i. Br., studied polysaccharides, i.e. starch, wood polysaccharides and, in conjunction with Schulz, the fine structure of cellulose⁹. Kohlschütter¹⁰, now in Darmstadt, investigated topochemical reactions using polyoxymethylenes. Batzer¹¹ has in recent years successfully continued Carothers' work on polyesters. Hengstenberg¹², Sauter¹³ and Plötzer¹⁴ carried out X-ray studies at different periods. Staudinger (M.)¹⁵ conducted morphological studies of macromolecular substances, and introduced light, ultraviolet and electron microscopy - and for some time now, phase contrast microscopy as well - into macromolecular chemistry. In addition, over the last 25 years in which almost 400 publications have appeared, she has collaborated in these and a series of books. She is the originator in particular of new considerations in respect of the relations between macromolecular chemistry and biology¹⁶.

I cannot mention here the names of all the individual assistants and graduate students but today I remember with gratitude the assistance of all those colleagues who have participated in expanding this field.

Since, as I explained, macromolecular compounds are built up according to the laws of Kekulé's structural theory in exactly the same manner as the low-molecular organic compounds, i.e. they are genuine organic com-

pounds but with particularly large molecules, the question arises whether there is any need at all to classify macromolecular chemistry as a new field of organic chemistry. It has been found, however, that owing to the size of the macromolecules, a whole series of new problems do actually arise here so that in many respects macromolecular chemistry differs substantially from low molecular chemistry.

Even the classification of the macromolecular compounds is based on other criteria than in low molecular chemistry: the naturally occurring macromolecular substances are conveniently treated separately from the fully synthetic compounds (Table 1).

Table I. Classification of macromolecular substances.

I. Substances occurring in nature

1. Hydrocarbons - rubber, guttapercha, balata.
2. Polysaccharides - celluloses, starches, glycogens, mannans, pectins, polyuronic acids, chitines.
3. Polynucleotides (nucleic acids).
4. Proteins and enzymes.
5. Lignins and tans (transition from low- to macromolecular substances).

II. Conversion products of natural substances

Vulcanized rubber, rayon, cellophane, cellulose nitrate, leather, lanital, galalith, etc.

III. Synthetic materials

Plastics (polyplastics) formed by
polymerization - buna, polystyrene, polymethacrylic ester.
polycondensation - bakelite, nylon, Perlon, Terylene.
polyaddition - polyurethane.

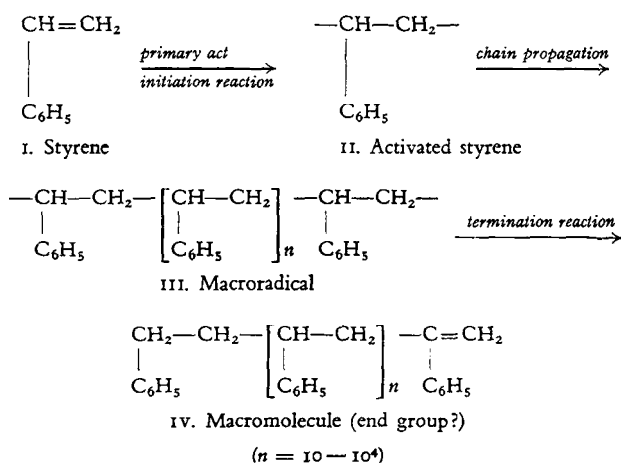
For the low molecular compounds such a division is unnecessary and irrelevant; the low molecular substances occurring in nature can largely be manufactured synthetically and these synthetic compounds are indistinguishable from the natural products. The situation is otherwise for the macromolecular compounds. It has so far proved impossible to build a macromolecular natural substance by a clear, stepwise synthesis from low molecular compounds. Thus synthetic polyisoprene is not identical with, say, natural rubber but has an essentially different constitution and hence other physical properties as well. In deriving macromolecular natural substances from vegetable and animal material the original macromolecules are in many cases modified to a greater or lesser extent by isolation and purification, and thus

the macromolecules examined are not the same as those formed by Nature. Problems of this type prevail for instance in the production of cellulose, starch, and many proteins. Low molecular products on the contrary can be isolated from natural products without modification. It is furthermore possible that Nature creates macromolecules of uniform size but positive proof of this fact has so far been found only in a few cases. In 1926 for example Svedberg¹⁷ made the astounding discovery that a number of respiratory proteins are monodisperse, i.e. that they are composed of uniformly large macromolecules. Recently a whole series of enzymes and hormone proteins have been crystallized so that here too the occurrence of natural products with uniformly large macromolecules is very probable¹⁸.

Against that the technically manufactured transformation products of natural macromolecular substances which can be termed semi-synthetic products are invariably polymolecular mixtures since the original macromolecules are broken down to a greater or lesser extent during processing. In all fully synthetic products, i.e. in plastics and fibres, there are also inseparable mixtures of polymer homologues. It is thus impossible to prepare completely uniform products by synthesis as was formerly considered necessary by the organic chemist to elucidate the constitution of organic compounds.

Macromolecular products are created in various ways. The first to deserve mention is polymerization, constituting a particular chain reaction such as is unknown in low molecular chemistry¹⁹ (Formula 1). Owing to the

Formula 1. Polymerization of styrene.

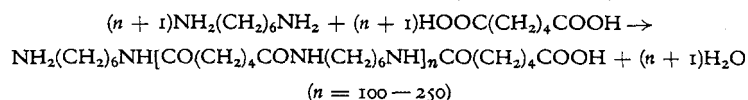


technical importance of the polymerisates, e.g. polystyrenes, polymethacrylic esters and polyvinyl chlorides, this reaction has been studied very thoroughly with reference to the kinetics and the influence of catalysts on the course of the polymerization²⁰.

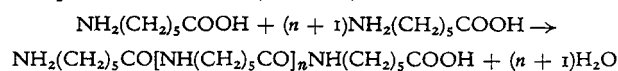
In addition, macromolecular substances can be produced by polycondensation, a process which has long been known to technology and the one whereby Baekeland secured the phenoplasts which are of unusual technical importance. This field was then further studied by Carothers²¹ and led to such technically valuable products as nylon (Formula 2).

Formula 2. Polyamides.

1. From hexamethylenediamine + adipic acid \rightarrow nylon (W. H. Carothers)



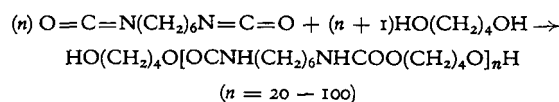
2. From ϵ -aminocaproic acid \rightarrow Perlon (P. Schlack)



A further technique to produce macromolecular compounds evolved by O. Bayer is polyaddition with diisocyanates (Formula 3).

Formula 3. Polyurethanes.

- e.g. from hexamethylenediisocyanate + 1,4-butanediol



In the most favourable case therefore, in the manufacture of fully synthetic products, uniform polymeric compounds are formed, i.e. mixtures of filamentary molecules of equal constitution but different length. Very recently, research conducted by Melville²³ and others showed that polymerization processes are frequently more complex than had formerly been assumed so that the resultant products are mixtures of polymer isomers.

Since most natural macromolecular substances as studied are polymolecular mixtures in common with all synthetic macromolecular substances, a

macromolecular substance must be identified by different criteria than a pure low molecular substance. Ostwald (Wi.)²⁴, in his Analytical Chemistry, has pointed out that the task of the analytical chemist is facilitated by the fact that the agreement of just a few properties of two substances is sufficient for regarding them as identical. This principle applies only for low molecular compounds in which, owing to the small size of the molecules or ions, relatively large differences in the properties occur, i.e. they differ abruptly from one compound to another. The situation is different for macromolecular compounds; a plastic such as, say, a polystyrene can be consistent with another polystyrene in a number of essential properties and still differ in composition. It is moreover also impossible to characterize and identify macromolecular substances by the melting point and by the mixed melting-point test, a technique which has contributed greatly to the rapid successes in the identification of natural substances in low molecular chemistry.

Initially identifying the constitution of macromolecular compounds seemed to be further complicated by the fact that they do not yield normal monodisperse solutions but that - if they dissolve at all - they mostly form polydisperse, colloidal solutions. The procedure for elucidating the constitution of organic compounds can again be referred to here: It consists in dissolving the particular compound after elementary analysis and then determining the size and finally the intrinsic structure of the dissolved particles by further studies. With completely insoluble substances occurring as a single aggregate only²⁵, details of the type of bond in the smaller groups in their molecules can in many cases be disclosed by decomposition; but the molecular weight of such a substance is indeterminable. Against that, however, it may not be inferred from the insolubility of a substance alone that it has a particularly

Table 2. New classification of disperse systems by the number of atoms.

Increasing degree of dispersion.

Coarse dispersions The particles are composed of more than 10^9 atoms, do not pass through filter paper and can be made visible microscopically. They are polydisperse.

Colloids The particles are composed of 10^3 to 10^9 atoms, pass through filter paper, cannot be resolved microscopically and cannot be dialysed. They are polydisperse or monodisperse.

Low molecular dispersions The particles are composed of 2 to 10^3 atoms, cannot be resolved microscopically, diffuse and dialyse readily. The molecules or ions of uniform substances are identical in structure and size.

high molecular weight, a fact which emerged during studies on amino-plasts²⁶ in the laboratory at Freiburg.

When considering the various modes of dispersion of organic substances in a liquid, it is expedient to indicate the size of the dispersed particles by the number of atoms they contain, the convention²⁷ adopted in Table 2. The particles of the low molecular organic compounds thus contain up to a maximum of 10^3 atoms and as a rule are identical with the molecules. The molecule concept is defined here in the same way as in low molecular chemistry: a molecule is the smallest particle in which all the atoms are linked by chief valences². It can readily be ascertained whether such particles contain not molecules but associations or double molecules, as applies with e.g. solutions of fatty acids in benzene.

The particles of colloidal size which are composed of 10^3 to 10^9 atoms can have a much more varied structure than the particles made up of fewer atoms (Table 3).

It follows from Table 3 that for one thing lyophobic colloids can occur which formerly roused special interest when Ostwald (Wo.)²⁹ drew attention to the "field of neglected dimensions" and pointed out that every substance can be broken down into particles of colloid size by appropriate

Table 3. Classification of colloidal solutions of organic substances.

| | <i>Behaviour to disper- sion media</i> | <i>Electrical charge</i> | <i>Viscosity of solutions</i> | <i>Example</i> |
|-------------------------------------------------------------------------------|------------------------------------------------|------------------------------|-----------------------------------------------------|--------------------------------------------|
| I. Dispersoid colloids | | | | |
| (a) suspensoids | lyophobic | charged | low | sugar in benzene |
| (b) emulsoids | lyophobic | charged | low | oils in water |
| II. Micellar colloids (formed by aggrega- tion of small mol- ecules) | lyophilic | mostly charged | high | soaps in water |
| III. Molecular colloids (solutions of macro- molecular substances) | lyophilic | charged or uncharged | low: spher- colloids high: linear colloids | glycogens, proteins cellulose, proteins |
| IV. Macromolecular as- sociations | lyophilic | charged or uncharged | low or high | proteins, simplexes, bio-colloids |

dispersion. A further group of colloids are the lyophilic colloids to which belong on the one hand the micellar colloids and on the other the solutions of macromolecular substances. Since macromolecules are the size of colloid particles they can dissolve in no other way than colloidally, even if the solvent is changed, whereas with micellar colloids, e.g. the soaps, low molecular disperse solutions are also possible in certain solvents. The solutions of macromolecular substances may hence also be termed molecular colloids³⁰.

Surprisingly, one group of macromolecular compounds, the linear macromolecular substances, exhibit in many respects properties like those of typical micellar colloids. In particular there is great similarity here to the soaps, the colloidal nature of which was recognized at the beginning of the century through the work of Krafft³¹, Zsigmondy³², McBain³³, and others. Since the solutions of linear macromolecular substances, however, differ substantially from the solutions of low molecular substances, it can be understood why, a few decennia ago, the colloid particles in these solutions of macromolecular substances were assumed to have a micellar structure similar to those in aqueous soap solutions (Table 4).

Table 4. Properties of various substances.

| <i>Properties</i> | <i>Low molecular substances</i> | <i>Linear macromolecular substances (e.g. rubber, starch, proteins)</i> | <i>Micellar colloids (e.g. soaps)</i> |
|-------------------------------------|---------------------------------|-------------------------------------------------------------------------|---------------------------------------|
| Dissolve: | without swelling | with swelling | with swelling |
| Dissolved particles are: | monodisperse | polydisperse | polydisperse |
| Solution is: | Newtonian | non-Newtonian | non-Newtonian |
| 1% solution is: | low viscous | high viscous | high viscous |
| Viscosity of solutions on standing: | constant | aging phenomena | aging phenomena |
| Dissolved particles are: | dialysable | undialysable | undialysable |

Initially therefore, the efforts of the workers studying rubber, cellulose, starch, and proteins were aimed at determining the size of the molecules making up these micells. A number of workers such as Karrer³⁴, Bergmann³⁵, Pummerer³⁶ and Hess³⁷ assumed them to be small molecules whereas Meyer and Mark³⁸ held that these micells consisted of rather long chief valence chains.

Notwithstanding this similarity in the behaviour of micellar colloids and linear molecular colloids which derives from the elongated shape of the colloid particles in both cases, there is a profound difference between the two groups: the particles of the micellar colloids are loose aggregates of small molecules, in the case of the molecular colloids they are the macromolecules themselves.

The proof was obtained by the conventional methods of organic chemistry, i.e. by determination of the "macroradicals". In this context the word "radical" is used in the meaning given to it by Liebig in his studies of the benzoyl radical. In many instances a polymeric compound can be transformed into derivatives of a different type without any change in the degree of polymerization of the compound in exactly the same way as small molecules can be transformed. A polymer compound can hence be transformed into polymer analogous derivatives, the transformation proving that all the basic molecules contained in the colloid particles of these polymeric compounds are linked together by chief valences, in other words the colloid particles are macromolecules. This proof becomes especially clear because out of a series of polymer homologues various ones can be transformed into polymer analogous derivatives. An explanation can be given with reference to cellulose.

The β -glucoside bond of the glucose radical in cellulose was established by the studies of Haworth³⁹ and Freudenberg⁴⁰; furthermore Sponsler and Dore⁴¹ demonstrated that the results of X-ray studies are consistent with the chain structure of cellulose. Subsequent studies then clarified the question whether the colloid particles in the solutions of celluloses and their derivatives have a macromolecular or micellar structure⁴².

Table 5. Comparison of the molecular weights of decomposed cellulose triacetates as determined by the osmotic and end-groups methods, and the K_m -constants of these compounds.

| <i>Osmotic method</i> | | <i>End-groups method</i> | | <i>Mean of</i> | $Z_{\eta} \cdot 10^3$ in | $K_m \cdot 10^4$ |
|-----------------------|-----------|--------------------------|-----------|----------------|--------------------------|------------------|
| \bar{M} | \bar{P} | \bar{M} | \bar{P} | \bar{P} | <i>m-cresol</i> | |
| 5,700 | 20 | 5,900 | 20 | 20 | 1.18 | 5.9 |
| 7,900 | 27 | 7,900 | 27 | 27 | 1.63 | 6.0 |
| 8,200 | 28 | 9,000 | 31 | 30 | 1.77 | 5.9 |
| 11,700 | 40 | 11,000 | 38 | 39 | 2.35 | 6.0 |
| 15,800 | 55 | 15,100 | 52 | 54 | 3.39 | 6.3 |
| Mean | | | | | | 6.0 |

In a polymer homologous series of decomposed low polymeric cellulose acetates, the molecular weight determined by the end groups agrees with that determined by the osmotic method, proof that unbranched filamentary molecules are present. The viscosity number Z_η of these compounds is proportional to the degree of polymerization as shown in Table 5.

The end-group molecular weight of higher polymer cellulose acetates can not be determined. The relations between the degree of polymerization determined by the osmotic method and the viscosity number Z_η are the same, however, as in the low molecular compounds appearing in Table 5, testifying that these high polymer cellulose acetates are dissolved in the macromolecular form and their chains are unbranched (Table 6).

Table 6. Determination of K_m -constants of higher polymeric cellulose triacetates in *m*-cresol.

| \bar{M} | \bar{P} | $Z_\eta \cdot 10^2$ | $K_m \cdot 10^4$ |
|-----------|-----------|---------------------|------------------|
| 22,800 | 79 | 5.28 | 6.7 |
| 36,000 | 125 | 8.35 | 6.7 |
| 41,700 | 145 | 6.65 | 6.6 |
| 49,000 | 170 | 9.85 | 5.8 |
| 81,000 | 280 | 18.05 | 6.4 |
| 93,000 | 325 | 21.45 | 6.6 |
| 106,000 | 370 | 24.50 | 6.6 |
| 225,000 | 780 | 52.10 | 6.7 |
| | | Mean | 6.5 |

With care, these cellulose acetates can be saponified to polymer analogous celluloses, so proving that both the cellulose acetates and the celluloses are present in solution in the macromolecular state⁴³ (Table 7).

Finally, with care being exercised, polymer homologous celluloses can be nitrated to polymer analogous cellulose nitrates with a mixture of nitric acid and phosphoric acid, so demonstrating the macromolecular structure of the cellulose nitrates⁴⁴ (Table 8).

The studies conducted at the Freiburg laboratory have frequently been concerned with determining macromolecular structure by polymer analogous transformations of this type. By that means it has been proved for further polysaccharides, i.e. starch's, glycogen⁴⁶, mannan⁴⁷, and for a number of plastics that the colloid particles in their solutions are identical with the ma-

Table 7. Transformation of cellulose triacetates to polymer-analogous celluloses.

| <i>Acetates in m-cresol</i> | | <i>Celluloses in Schweizer's reagent</i> | | <i>Z_η-acetates</i> | <i>K_m · 10⁴</i> |
|---------------------------------------|------------|------------------------------------------|-------------|---------------------------------|---------------------------------------|
| <i>Z_η · 10²</i> | <i>DP*</i> | <i>Z_η · 10²</i> | <i>DP**</i> | <i>Z_η-celluloses</i> | |
| 3.4 | 54 | 2.8 | 56 | 1.21 | 5.0 |
| 18.0 | 285 | 15.3 | 305 | 1.17 | 5.3 |
| 21.4 | 340 | 17.6 | 350 | 1.22 | 5.2 |
| 60.4 | 960 | 47.9 | 955 | 1.26 | 5.0 |
| 74.4 | 1,180 | 58.3 | 1,165 | 1.27 | 5.0 |
| 104.5 | 1,660 | 84.0 | 1,680 | 1.24 | 5.1 |
| | | | Mean | 1.25 | 5.1 |

* Calculated from Z_{η} of column 1 with $K_m = 6.5 \cdot 10^{-4}$

** Calculated from Z_{η} of column 3 with $K_m = 5 \cdot 10^{-4}$

macromolecules. It is surprising that with these molecules, some of which are very large and complex, reactions can be conducted which are customary with molecules of lower molecular compounds. Such polymer analogous transformations hence provide an impressive instance of the stability of the macroradicals which is also of significance for the substances of living cells.

The question now arises of the origin of the frequent instability and changeability in the viscosity of macromolecular substances in solution. These "aging phenomena" arise because even slight amounts of low molecular substances are sufficient, chiefly in the presence of atmospheric oxygen,

Table 8. Transformation of celluloses into polymer-analogous cellulose nitrates.

| <i>Cellulose in Schweizer's reagent</i> | | <i>Cellulose nitrates in acetone</i> | |
|-----------------------------------------|----------------------------------------------------|---------------------------------------|-----------------------------------------------------|
| <i>Z_η · 10²</i> | <i>DP with K_m = 5 · 10⁻⁴</i> | <i>Z_η · 10²</i> | <i>DP with K_m = 11 · 10⁻⁴</i> |
| 3.8 | 76 | 8.5 | 77 |
| 7.6 | 152 | 15.0 | 135 |
| 16.8 | 336 | 34.0 | 310 |
| 24.0 | 480 | 51.0 | 460 |
| 35.8 | 716 | 74.0 | 670 |
| 67.5 | 1,350 | 161 | 1,460 |
| 80.0 | 1,600 | 188 | 1,710 |
| 100 | 2,000 | 200 | 1,800 |
| 168 | 3,400 | 390 | 3,540 |

to decompose the linear macromolecules, leading to a profound change in the solution viscosity. This is shown in Table 9.

Table 9.

| | | |
|-----------------------------------|------------------|-----------------------------------------|
| 1 mol cellulose (DP 3,000) | + 4 atoms oxygen | → 2 mol cellulose (DP 1,500) |
| 486,000 g cellulose (DP 3,000) | + 64 g oxygen | → 2 × 243,000 g cellulose (DP 1,500) |
| 7.5 g cellulose (DP 3,000) | + 1 mg oxygen | → 2 × 3.75 g cellulose (DP 1,500) |

Initially, as was the case for instance with rubber, these aging phenomena were particularly obscure because under certain conditions oxygen decomposes the filamentary molecules but can also link them together, this becoming apparent in an increase of viscosity and, should the linking of the filamentary molecules proceed further, it causes the soluble rubber to change into insoluble rubber. For this reason even polymer analogous transformations involving macromolecular substances are mostly to be conducted only under special experimental conditions since atmospheric oxygen for instance must be completely excluded. The tests are also complicated by the fact that the transformation products cannot be purified since all substances are polymolecular and reprecipitation together with purification would lead to a change in the composition of the polymolecular mixture. These complications do not exist where low molecular substances are involved.

With the most important group of macromolecular compounds, the proteins and nucleic acids, scarcely any polymer analogous transformations have so far been performed; here too it is difficult to produce polymer homologous series. The size and structure of the macromolecules have to be determined by different methods from those applied with the polysaccharides, rubber, and the plastics. The molecule concept as formulated for homopolar organic compounds is not applicable here without limitation since besides chief valences, very powerful secondary valences also participate in the structure of the particles.

The proof for the macromolecular structure of colloid particles is of fundamental importance since it signifies that these colloids cannot be considered in terms of the colloid doctrine as variable associations of small molecules but rather as macromolecules which must be treated by the methods of organic chemistry in common with molecules of low molecular substances⁴⁸.

There are still further profound differences between macromolecular and low molecular compounds: these are based primarily on the fact that the shape of the macromolecules affects the physical and chemical properties of the substances considerably more strongly than is the case with the low molecular compounds. Whereas, for example, normal nonane with elongated molecules, and tetraethylmethane with spherical molecules, both hydrocarbons having the composition C_9H_{20} , scarcely differ in terms of their properties, a glycogen in which 5,000 glucose radicals are linked to form a sphere has properties differing fundamentally from those of a cellulose in which the same number of glucose radicals are arranged in a long chain. This state of affairs led to the macromolecular substances being classified into two large groups, spheromacromolecular substances, i.e. substances with spherical molecules, and linear macromolecular substances with filamentary molecules. These two classes are, of course, bridged by transitions: a large number of natural and synthetic substances have heavily branched macromolecules, e.g. starch^{4,5}. Table 10 indicates the significant bearing of the shape on the physical properties of natural macromolecular substances⁴⁹.

Table 10. Spherical and filamentary polysaccharides and proteins.

| | <i>Spherocolloids</i> | <i>Linear colloids</i> |
|---------------------------|------------------------------------------|-----------------------------------------------------------------------|
| Polysaccharides | glycogen | cellulose, pectin |
| Proteins | ovalbumin, haemoglobin, lactoglobulin | collagen, myosin |
| Appearance in solid state | powdery | fibrous, tough |
| Swelling properties | fail to swell | swell considerably |
| Viscosity of 1% solution | low viscous solutions | high viscous gel solutions |
| Type of solutions | Newtonian | non-Newtonian, linear macromolecular or polyionic viscosity phenomena |
| Flow birefringence | none | increases with length of filamentary molecules |
| Osmotic pressure | in dilute solution obeys Van 't Hoff law | deviates from Van 't Hoff law |
| Diffusion | obeys Fick law | deviates from Fick law |

In appearance, solubility, and in their further behaviour, macromolecular substances with spherocolloid molecules scarcely differ from low molecular substances; only the determination of the molecular weight proves that macromolecules are involved. The striking properties of macromolecular substances which, as listed in Table 4, caused a different type of micellar structure to be assigned to these compounds, occur only with the linear macromolecules; these include the natural and fully synthetic fibres, the rubber-elastic substances and many of the most important plastics. Linear macromolecular substances with long filamentary molecules behave in a manner alien to low molecular substances: inclusion and swelling phenomena, high solution viscosity, abnormal flow behaviour, etc. Since the constitution of these substances is known, their striking behaviour can be ascribed to the length of the filamentary molecules. A comparison of various examples of a polymer homologous series shows that as the filamentary molecules become longer, their properties change so profoundly that the earlier concepts which led to the conclusion that the units at the beginning and at the end had a completely dissimilar structure (Table 11) can be appreciated.

Table II. Relation between physical properties and mean degree of polymerization (DP) of polymer homologous celluloses.

| | DP | Appearance | Fibre and film forming properties | Solubility and swelling in Schweizer's reagent | Viscosity of 1% solutions in Schweizer's reagent |
|---------------------|----------|-------------|-----------------------------------------------------------|------------------------------------------------|--------------------------------------------------|
| Oligosaccharides | 1-10 | powdery | triturable, forms neither fibres nor films | rapidly soluble, without swelling | low viscous sol solutions |
| β -Cellulose | 10-100 | powdery | partially solid, forms neither fibres nor films | dissolves without swelling | slightly viscous sol solutions |
| α -Cellulose | 100-500 | fibrous | solid, forms fibres and films | dissolves with swelling | viscous gel solutions |
| α -Cellulose | 500-3000 | long fibres | very solid and tough, very readily forms fibres and films | dissolves slowly with strong swelling | gel solutions of very high viscosity |

It was therefore particularly difficult to study these linear macromolecular substances. Even to determine the molecular weight, for example, it was not possible to apply the customary physical techniques such as the osmotic, diffusion, or Svedberg ultracentrifuge methods until the abnormal behaviour of the solutions of these substances could be clarified⁵⁰.

The viscosity behaviour of the linear macromolecular substances is particularly striking. Whereas Einstein's law applies to the spheromacromolecular substances such as ovalbumin or glycogen, in the case of solutions of substances with filamentary molecules, the viscosity of solutions of equal concentration increases with the chain length, and with some of these substances, especially polysaccharides, there is a proportionality between the viscosity number Z_η , and the chain length n or the degree of polymerization P of filamentary molecules. This viscosity number is the specific viscosity of a solution, i.e. the increase in viscosity caused by 1 g in one litre, or else its limit value. Since viscosity measurements are simple to perform, this method has been extensively adopted in technology to determine e.g. the degree of polymerization of celluloses and cellulose derivatives, as this parameter has a considerable bearing on the fibre properties as shown in Table 11. With other linear macromolecular substances such as e.g. the polyesters¹¹ and many polyvinyl derivatives, the relation between viscosity number Z_η and degree of polymerization is not as simple as with the polysaccharides, although there is a functional relation corresponding to an equation formulated by Kuhn⁵¹ (Table 12).

Table 12. Viscosity relations.

| | |
|-------------------------------------------------------|--------------------------------------------------------------------------|
| $\eta_r = 1 + K \cdot \Phi$ | Einstein, 1906 |
| $\eta_r - 1 = \eta_{sp}$ | Staudinger and Heuer, 1930 |
| $\lim_{c \rightarrow 0} \frac{\eta_{sp}}{c} = Z_\eta$ | |
| $Z_\eta \cdot s = 0.0025$ ($s = \text{density}$) | e.g. valid for ovalbumin |
| $Z_\eta = K_m \cdot P$ | Staudinger and Heuer, 1930, e.g. valid for cellulose and its derivatives |
| $Z_\eta = K_m \cdot P^x$ | Kuhn, 1936, e.g. valid for polyesters |

The reasons are as follows: the filamentary molecules of a linear macromolecular substance are usually elongated in the solid crystalline state. The length of the elementary units and hence the length of the filamentary mol-

ecules can be determined by X-ray examination, e.g. in the case of cellulose. On dissolution, owing to vibrations and intramolecular forces of attraction between the individual groups of the filamentary molecule, the latter becomes convolute to a greater or lesser extent depending on the temperature and also on the type of solvent. Thus the filamentary molecules in good solvents are more elongated than in poor solvents; in the former the viscosity number of a substance is higher than in a poor solvent. Kuhn⁵² states that the entanglement of a filamentary molecule can be so pronounced in a poor solvent that the molecule assumes an almost spherical configuration such as has been experimentally determined with the polyisobutylenes⁵³. A filamentary molecule would adopt that configuration in the gaseous state although in practice this state is unattainable, since the boiling point of all macromolecular substances lies far beyond the point at which they decompose.

Besides these reversible changes in shape which are governed by the nature of the filamentary molecule and the type of the solvent, chemical action also brings about irreversible changes in shape which permanently affect the physical properties of a linear-macromolecular substance. Thus it is common knowledge that owing to its long, filamentary molecules, rubber yields highly viscous solutions with swelling. Against this, the solutions of chlorinated rubber, which is used as a paint, are of relatively low viscosity and therefore it was originally assumed that in the transformation from rubber to chlorinated rubber the long filamentary molecules were decomposed. Such is not the case as the degree of polymerization of chlorinated rubber is approximately the same as that of rubber⁵⁴. Thus, when rubber is converted into chlorinated rubber, no decomposition takes place but rather a strong, chief valence cyclization which induces a permanent convolution of the filamentary molecules (Table 13).

Table 13. Polymer-analogous transformation of rubber and balata to chlorination products.

| | \bar{M} | \bar{P} | Z_n | $K_m \cdot 10^4$ |
|-------------------------|-----------|-----------|-------|------------------|
| Rubber | 182,000 | 2,700 | 0.46 | 1.7 |
| Chlorinated rubber | 410,000 | 2,600 | 0.077 | 0.30 |
| Balata | 99,000 | 1,450 | 0.188 | 1.3 |
| Hydrochlorinated balata | 135,000 | 1,400 | 0.088 | 0.63 |
| Chlorinated balata | 250,000 | 1,300 | 0.041 | 0.32 |

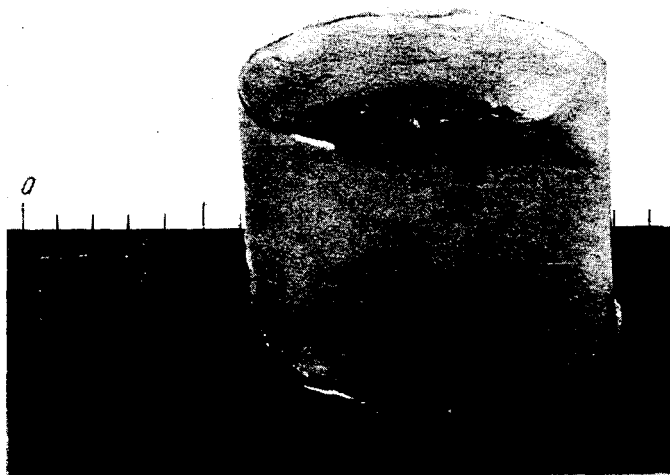


Fig. 1. Swelling of a piece of polystyrene with divinyl bonds. Before swelling (*left*).
After swelling in benzene (*right*).

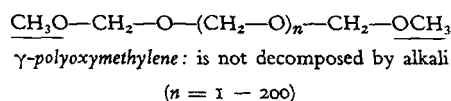
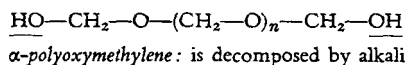
It is - as already mentioned - characteristic of the chemistry of macromolecular materials that the smallest amounts of substances are capable of modifying profoundly their physical properties. Hence a 0.0025% addition of divinyl benzene to styrene is sufficient during polymerization to link the chains of the polystyrene by divinyl benzene bonds⁵⁵. Soluble polystyrene with its unlimited swelling capacity is thus transformed into a variety with limited swelling capacity which absorbs solvents by solvation and so swells without altering its shape (Fig. 1) and without being able to dissolve.

The replacement of a hydroxyl group in low molecular compounds by a methoxyl group alters the physical and, above all, the chemical behaviour of the compound considerably. The same applies also to macromolecular substances except that the percentage proportion of a methoxyl end group in the macromolecule can be so small that it readily escapes detection. Auerbach and Barschall⁵⁶ described two polyoxymethylenes: one is soluble in sodium hydroxide, the other insoluble, yet they are identical in appearance. The product soluble in sodium hydroxide is a polyoxymethylene dihydrate, the insoluble product a polyoxymethylene dimethylether⁵⁷ (Formula 4).

The slight percentage methoxyl end-group content thus blocks the decomposition of the chains by sodium hydroxide. This reagent can only at-

tack hydroxyl groups and so dissolve polyoxymethylene dihydrate. In biological processes as well, a slight percentage change in a macromolecule can bring about profound changes in the chemical and physiological behaviour of the macromolecular substance.

Formula 4. Formulae of polyoxymethylenes.



Possibly the most important distinction between low molecular and macromolecular compounds is that the latter can exhibit properties which cannot be predicted even by a thorough study of the low molecular substances. This may be illustrated by comparing the organic molecules with buildings in which the bricks must be joined together systematically. With a few bricks it is impossible to erect a great variety of buildings; nevertheless, provided that 10,000 or 100,000 bricks are available it is quite possible to construct the most diverse buildings, viz. houses, halls, etc., the special construction of which cannot simply be predicted from the buildings comprising few bricks.

One such new type of behaviour of macromolecular substances are, for example, the swelling phenomena of the linear macromolecular substances caused by the solvation of the long filamentary molecules on the addition of solvent without immediately being able to go into solution. These swelling phenomena are complicated, as has been described, in that linking of the filamentary molecules induces a substance with unlimited swelling capacity to change into a substance of restricted swelling capacity⁵⁵, this also being a very potent factor with proteins. A further instance here are inclusion phenomena. Inclusion is an indirect swelling of linear macromolecular substances with liquids that are not solvents. They have mainly been studied in the case of cellulose, between the filamentary molecules of which inert liquids such as benzene, carbon tetrachloride, and others can be embedded. It is noteworthy that these liquids cannot be altogether eliminated from the linear macromolecular substance even under a high vacuum; they are held mechanically between the filamentary molecules of the substances. As a

Table 14. Amount of solvent included in mercerized cotton (DP 1,600) after drying for two days under high vacuum at 100°C.

| <i>Included liquids</i> | <i>Amount included [%]</i> | <i>Number of glucose anhydride mols to one mol inclusion medium</i> | <i>Acetyl content [%] after one day's treatment with acetic acid anhydride-pyridine at 60°C</i> |
|-------------------------|----------------------------|---------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| A. Pure cellulose | | | |
| Water | 0.0 | — | 0.3 |
| Methanol | 0.3 | — | 1.3 |
| B. Inclusion cellulose | | | |
| Ethyl alcohol | 2.4 | 12 | 21.2 |
| Acetone | 2.5 | 14 | 21.3 |
| Pyridine | 6.4 | 7 | 23.6 |
| Cyclohexane | 8.1 | 6 | 20.1 |
| Benzene | 3.4 | 14 | 19.1 |
| Carbon tetrachloride | 7.2 | 12 | 19.4 |

result of this inclusion, however, the reactivity of cellulose is appreciably raised⁸ (Table 14).

A particularly significant phenomenon with linear macromolecular substances is a characteristic state of dissolution which is impossible with spheromacromolecular and low molecular substances: the state in which the filamentary molecules are completely solvated, i.e. essentially dissolved, but owing to their large bulk, their range of action, they have no free mobility. The term "gel solution" has been proposed for this characteristic state of dissolution which is intermediate between the normal state of dissolution and that of swelling^{5,9}. The solutions of cellulose, cellulose derivatives and plastics as used technically are gel solutions.

It will be the task of macromolecular chemistry to examine further these new, characteristic properties which are governed by the size and configuration of the macromolecules since it will thus be possible to gain fresh insight into biological processes as well.

The existence of macromolecules and the steadily deepening knowledge of their properties have revealed the nature of the building units which the living cell requires to create matter¹⁰. The existence of macromolecules makes possible the vastly wide variation of the substances required; thus, for example, the very number of the isomers in protein molecules is practically infinite. Assuming a protein of molecular weight 100,000 and com-

posed of 20 different amino acids, the number of its isomers is 10^{1270} . The size of this number becomes clear when compared with the number of molecules of water present in the seas of the earth - a mere 10^{46} (Table 15).

Table 15.

Number of isomers of a protein having a molecular weight 105; the protein molecule composed of 50 molecules of each of 20 different amino acids.

Number of isomers: 10^{1270} .

For comparison the number of molecules of water in the seas of the earth:

Volume of the seas is about 1.3×10^{24} cm³; 18g water contain 6×10^{23} molecules.

The seas thus contain about 4×10^{46} molecules.

It is thus possible by isomerism alone to create an infinite number of substances. This number is increased still further by variation in the configuration of the macromolecules while they are being built, or else by the influence of their environment. So, each living organism can create its own nucleic acids, protein molecules, etc. This conclusion is necessary since every organism, and every human being too, differs chemically from another.

Associated with this boundless profusion of matter in the macromolecular sphere, in contrast, is a remarkable stability of the macromolecules, a stability which is governed by their structure as organic compounds in compliance with the laws of Kekulé's structural theory. That alone is capable of satisfying the "inconceivably strict demands on the integrity of the germ plasm" which are applied to the normal process of development of an organism⁶⁰. This stability of the macromolecules, associated with their reactivity, supplies the living substance with the necessary basis for so specific a process as that of heredity.

The known facts of macromolecular chemistry show further that an individual macromolecule is still not "living", however large it is and however complex its structure. On the contrary, the term is relevant to a certain amount of substance comprising numerous macromolecules with the constituent small molecules combined together in strictly prescribed order, an "atomos" of living matter¹⁶ which is indivisible without losing its "livingness". Living nature supplies the answer to the question how large such an "atomos" has to be in the form of the various germ cells, for nothing can be removed from such a cell, whether a spore or a fertilized ovum, otherwise no normal organism can be formed from it. One of the smallest units capable of self-propagation is, for example, a bacterial spore. The following estimate

Table 16. A bacterial spore of 0.124 μ diameter weighs 10^{15} g (sp.gr. = 1) and after removal of 50% water content comprises $5 \cdot 10^7$ atoms.

| Number of molecules when spore consists of | | | |
|--------------------------------------------|----------------------------------|---|-------------------|
| 30% | macromolecules with 10^6 atoms | = | 15 macromolecules |
| 30% | „ „ 10^5 „ | = | 150 „ |
| 10% | „ „ 10^4 „ | = | 500 „ |
| 10% | molecules „ 10^3 „ | = | 5,000 molecules |
| 10% | „ „ 10^2 „ | = | 50,000 „ |
| 10% | „ „ 10 „ | = | 500,000 „ |

may afford an idea of what numbers of macromolecules and molecules are the necessary minimum for "livingness" here (Table 16).

In contrast to former opinions one of the smallest living units thus requires a quantity of substance.

In this way macromolecular chemistry appears today to fit between low molecular organic chemistry and cytology. It is the connecting link between them, growing systematically out of low molecular chemistry but, with the incomparably larger wealth of its chemical scope, forming living matter. In addition, over and above the quantitative laws of pure chemistry, macromolecular chemistry makes use of a number of qualitative correlations: those of shape and of the associated configurational scope, up to the level of the "atoms" of living substance, on which the game of Life ensues.

In the light of this new knowledge of macromolecular chemistry, the wonder of Life in its chemical aspect is revealed in the astounding abundance and masterly macromolecular architecture of living matter.

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