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THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

ASYMMETRIC SYNTHESES AND THEIR BEARING UPON THE DOCTRINE OF VITALISM[1]

IN the history of the development of any science certain discoveries stand out boldly as epoch-making in importance. In the domain of organic chemistry the observations of Liebig and Wöhler (1826) that cyanic and fulminic acids have the same percentage composition, rank with this class of discoveries; for the establishment of this fact laid the foundation for the development of the principle of isomerism. Likewise to this class belongs the investigation of Wöhler (1828) in which he proved that urea results from the spontaneous rearrangement of ammonium cyanate, a discovery of no great significance in itself, but of the greatest importance when regarded from its bearings upon the ideas concerning organic compounds prevalent in the first quarter of the nineteenth century; for it carried with it the abandonment of the universal belief that compounds elaborated within the living organism can not be prepared synthetically by laboratory methods. Following Wöhler's classical discovery came those brilliant investigations of Pasteur (1844–49) on the tartaric acids which led to the development of our modern ideas concerning space-isomerism or stereoisomerism.

Since it is my purpose to deal with a certain phase of stereo-isomerism I will re-

[1] Address of the vice-president and chairman of Section C, Chemistry, American Association for the Advancement of Science, New York, December, 1916.

view briefly a few of the important discoveries that led up to the investigations of Pasteur. These discoveries are outlined in the historical introduction of Pasteur's lectures delivered before the Chemical Society of Paris in 1860.

The fact that a ray of light in passing through a crystal of Iceland spar is divided into two rays had been known for many years, but it remained for Huygens and Newton in 1678 to point out that the ray of light is altered in its properties as it passes through the crystal. Later in 1808 Malus was able to show that light was similarly altered in properties by being reflected from any object and designated this change in properties by the term "polarization." Malus followed up this discovery with a number of important observations, but his early death at the age of 37 ended his brilliant career. The work, however, was continued by two young physicists Arago and Biot, and the latter devoted a long life primarily to the study of polarized light and its attending phenomena. It was Biot who observed that plates cut from certain quartz crystals rotate the plane of polarization to the right while similar plates cut from other quartz crystals rotate it to the left. In 1815 he announced to the Société philomatique the very important discovery that this property of rotating the plane of polarization is not confined to solids; for solutions of certain organic compounds, including sugar, camphor and tartaric acid likewise cause a rotation of the plane. Biot's studies led him to the definite conclusion that while both the quartz crystal and the sugar solution rotate the plane of polarization, the rotation in the two cases is due to different causes. In the former case the crystalline structure must be the influencing factor, for silica in the amorphous state does not rotate the plane of polarization. On the other hand, the ability of the sugar solution to rotate the plane of polarization must lie in the structure of the sugar molecule.

Another important observation in connection with this general subject was made by Hauy and Weiss, who noted in their study of quartz crystals that some of the crystals possessed certain faces truncating the upper edge of the prism face. They observed, moreover, that these faces or planes did not occupy the same position on all crystals; that in some, the plane appeared on (say) the right upper edge while in others it occupied a similar position on the corresponding left edge. With this difference as a basis, the crystals could be divided into two groups, the members of which are related to each other as object is to image, or as the right hand is to the left. It was Herschel who suggested (1820) that the difference in the optical activities of the quartz crystals, as noted above, might be connected with the position of these truncating planes on the crystal, and that of the two groups of crystals referred to, the members of the one group might rotate the plane of polarization in the one direction while the members of the other group might rotate it in the opposite direction. Experiments soon proved the verity of Herschel's suggestion.

THE INVESTIGATIONS OF PASTEUR BEARING UPON ASYMMETRY

The above account gives briefly the state of the knowledge of polarization when Pasteur began his now classical investigations. In order to familiarize himself with crystals, Pasteur decided to repeat some important research in this field of study—a method which may well be recommended to all who are in training for research work. For this purpose he chose the investigations of de La Provostaye on the tartaric acids published in 1841. In this study Pasteur soon

discovered what had escaped the eyes of even so keen an investigator as de La Provostaye, namely, that the crystals of the tartrates possessed truncating planes analogous to those observed in the quartz crystals. He found, however, that in the case of the crystals of the salts of the optically active tartaric acid (dextro-tartaric acid) these planes all occupied the same relative position so that the crystals were all identical. On the other hand, the crystals of the salts of the optically inactive tartaric acid (racemic acid), like the quartz crystals, could be divided into two groups according to the position of the planes, the members of the one group being related to those of the other as object is to image. It was but a step to show that, of the two groups of the crystals formed by the salts of the inactive acid, the one group rotated the plane of polarization to the right while the other rotated it an equal amount to the left; that the acid prepared from the group of crystals which rotated the plane of polarization to the right was in every way identical with the well-known dextro-tartaric acid and that the acid prepared from the remaining group of crystals was identical with the dextro acid in every respect except that it was levorotatory.

Here then, lay the secret of the optical inactivity of racemic acid, as well as the secret of the relation of the racemic acid to the ordinary active tartaric acid.

Pasteur realized the importance of his results. Vallery-Radot in his fascinating life of Pasteur gives a vivid account of the discovery. After referring to the final experiment in which Pasteur had tested the activity of the two sets of crystals in the polarizing apparatus, the biographer continues:

His excitement was such that he could not look at the apparatus again; he rushed out of the laboratory, not unlike Archimedes. . . . Never was there greater or more exuberant joy on a young

man's lips. He foresaw all the consequences of his discovery. The hitherto incomprehensible constitution of paratartaric or racemic acid was explained; he differentiated it into right-hand tartaric acid, similar in every way to the natural tartaric acid of grapes, and left-hand tartaric acid. These two distinct acids possess equal and opposite rotatory powers, which neutralize each other when these two substances, reduced to an aqueous solution, combine spontaneously in equal quantities.

The discovery was received with the greatest interest by the French scientists. The story is well known of how Biot, then an old man, wishing to learn more about the work before presenting it to the French Academy, invited Pasteur to repeat the experiments in his laboratory, using solutions which Biot himself had prepared, and how upon the completion of the experiments he grasped Pasteur's hand, saying:

My dear child, I have all my life so loved this science that I can hear my heart beat with joy.

Pasteur had connected the different effects of the dextro- and levo-tartaric acids with the asymmetrical character of their molecules. I quote from him:

We know, in fact, on the one hand, that the molecular arrangement of both tartaric acids is asymmetric; on the other, that they are entirely the same, with the exception that the asymmetry is shown in opposite senses. Are the atoms of the dextro acid arranged in the form of a right-handed spiral, or are they situated at the corners of an irregular tetrahedron, or do they have some other asymmetric grouping? This we do not know. But without doubt the atoms possess an asymmetric arrangement like that of an object and its reflected image.

Following the work of Pasteur, Wislicenus in 1873 made an extended study of the different isomeric lactic acids and concluded that the existence of these could be explained only upon the assumption that their differences are due, not to different groups of atoms, but to a different arrangement of the same groups in space.

It remained for van 't Hoff and Le Bel in 1874 to propose a theory which gives a satisfactory explanation of the facts. These

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two scientists working independently reached almost identical conclusions at about the same time, van't Hoff presenting his views in a brochure published at Utrecht in September, 1874, while Le Bel's article appeared two months later in the November issue of the *Bulletin de la Société Chimique de Paris*. In accordance with the views advanced by van't Hoff and Le Bel every molecule containing a carbon atom attached to four different groups (a so-called asymmetric carbon atom) may exist in two forms related to each other as object is to image. The one form of molecules rotates the plane of polarization to the right, the other form rotates it an equal extent to the left. It follows, therefore, that a compound containing an asymmetric atom may be expected to exist in three forms: the dextro or *d*-form composed of those molecules which rotate the plane of polarization to the right; the levo or *l*-form composed of those molecules which rotate the plane of polarization to the left; and the inactive or racemic form which consists of a true chemical combination of the two kinds of molecules in equal quantities. It is also possible to have equimolecular inactive mixtures of the dextro and levo forms.

This theory of van't Hoff and Le Bel, well known and therefore but briefly sketched, was vigorously opposed and even ridiculed when first advanced. Kolbe referred to it in the following terms:

A Dr. J. H. van't Hoff, stationed at the veterinary school at Utrecht, as it appears, finds no pleasure in exact chemical investigations. He has deemed it easier to mount Pegasus (evidently borrowed from the veterinary school) and in his "Chemistry in Space" to announce how the atoms lying about in the universe, appeared to him from the chemical Parnassus which he had climbed in his bold flight. . . . To criticize this writing even in a half way thorough manner is not possible, because the fantastic absurdities are entirely lacking in actual foundation and are entirely incomprehensible to the sober-minded investigator.
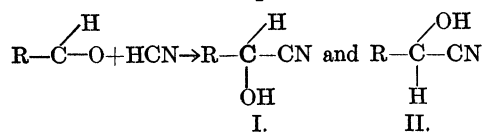
Notwithstanding these criticisms the theory advanced by van't Hoff and Le Bel has stood the test of experiment better perhaps than any other theory ever advanced within the domain of organic chemistry and has been a most potent factor in the development of stereo-chemistry.

THE SYNTHESIS OF ASYMMETRIC COMPOUNDS

To me the most interesting problem belonging to the general subject of stereo-chemistry is that of synthesizing compounds containing an asymmetric group. As stated above, compounds containing such a group may exist in three forms. The early attempts to synthesize such compounds, however, always resulted in the production of equal quantities of the dextro and levo forms, which either remained as mixtures or combined to produce the racemic form. As a result, the product obtained was always optically inactive. There is nothing remarkable in this result. Indeed, it is just what one would expect; for so far as one is able to judge the chances for the atoms to combine in one of the two possible ways is the same as the chances for them to combine in the other way. It would naturally follow, therefore, that the two possible forms of molecules will be produced in numbers that are equal, or are at least approximately so. The remarkable fact is not, therefore, that the synthetic compound of the laboratory is optically inactive or so nearly so that its activity can not be detected by any instruments yet devised, but rather that compounds occurring in nature and containing an asymmetric group with very few exceptions always occur in the active form. In other words, nature's synthetic methods result apparently in the formation of the dextro or of the levo form alone, while the synthetic methods of the laboratory always lead to the production of the two forms in equal quan-

tities. This striking difference between the natural and the laboratory synthesis has attracted much attention and extended investigations have been made in recent years to solve the mystery. Nevertheless, the problem of building up from its elements the dextro or the levo form alone or the one form in excess of the other so that the resulting product is optically active, remains to-day as in the beginning, an unsolved problem.

While the synthesis of either the dextro or the levo form alone of an asymmetric compound from its elements or from optically inactive materials has never been accomplished, nevertheless, it is entirely possible to build up an asymmetric compound if we employ another already existing optically active compound as an agent for effecting the synthesis. That such a procedure is possible was shown by Fischer in 1889 in the course of his celebrated investigations on the sugars. It had long been known that the so-called aldose sugars combine directly with hydrocyanic acid. This addition introduces a new asymmetric carbon atom into the compound:

$$R-\underset{\underset{\text{I.}}{\overset{|}{O}H}}{\overset{\overset{\displaystyle H}{\diagup}}{C}}-O+HCN \rightarrow R-\underset{\underset{\text{}}{\overset{|}{O}H}}{\overset{\overset{\displaystyle H}{\diagup}}{C}}-CN \text{ and } R-\underset{\underset{\text{II.}}{\overset{|}{H}}}{\overset{\overset{\displaystyle OH}{\diagup}}{C}}-CN$$

We might naturally expect that the two possible forms (I. and II.) of the new asymmetric group will be produced in equal amounts. Fischer found, however, that when hydrocyanic acid combines with *d*-glucose, both forms of the resulting cyanogen derivative are indeed obtained, but that the one form is obtained in excess of the other. When the action is carried on with *d*-mannose the one form only is produced. This result is readily explained upon the very reasonable assumption that the manner of the addition of the hydrocyanic acid to the sugar molecule is influenced by the forces exerted by the asymmetric groups already present in the sugar molecule. In the absence of such modifying forces, that is, in compounds which do not contain asymmetric groups, the two possible forms are produced in equal quantities, but in the presence of such asymmetric groups the two forms may be produced in unequal amounts.
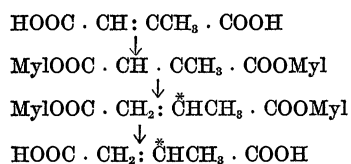
Now it will readily be noticed that this observation of Fischer suggests a possible way of effecting the synthesis of an optically active body from its constituent elements. For example, if one could find some method for splitting off from the molecule, the new asymmetric carbon group added to *d*-mannose in such a way that the resulting compound would contain this asymmetric group, then it is evident that the compound so produced would be optically active since it would consist of the one form only. Thus a synthesis of an optically active compound would have been effected, although it would have been made possible through the influence of a previously existing optically active compound.

While it has not been found possible to split off the newly formed asymmetric group resulting from the addition of hydrocyanic acid to *d*-mannose, nevertheless the synthesis of a number of optically active compounds has been accomplished through the application of this general principle. Such a synthesis is generally termed an asymmetric synthesis. However, such a synthesis, accomplished as it is through the assistance of an already existing optically active compound, is only partial and I shall designate it in the discussion that follows as a partial asymmetric synthesis. This term, as I shall use it, signifies the synthesis of either the dextro or levo form alone, or of the two forms in unequal amounts, effected through the assistance of an already existing optically active compound. It is

evident, then, that the production of the two forms in equal amounts with their subsequent separation from each other—a task often easily accomplished—does not constitute a complete asymmetric synthesis.

A brief discussion of the more important attempts to effect partial asymmetric syntheses follows:

1. The first serious attempt to effect a partial asymmetric synthesis was made by Cohen and Whitely in 1901. An optically active ester was prepared by heating an unsaturated acid (mesaconic acid was used) or its derivatives with levo-menthol. The resulting ester was then reduced, whereby one of the carbon atoms present was rendered asymmetric. The ester was then saponified so that the active menthyl group was eliminated, leaving methyl succinic acid containing the newly formed asymmetric group. The course of the reactions is shown in the following equations in which the abbreviation Myl represents the menthyl group, while the newly formed asymmetric carbon atom is designated by a star:

$$HOOC . CH : CCH_3 . COOH$$
$$\downarrow$$
$$MylOOC . CH . CCH_3 . COOMyl$$
$$\downarrow \quad *$$
$$MylOOC . CH_2 : \overset{*}{C}HCH_3 . COOMyl$$
$$\downarrow \quad *$$
$$HOOC . CH_2 : \overset{*}{C}HCH_3 . COOH$$

The resulting product, however, was inactive, showing that the dextro and levo forms had been produced in equal amounts. Pyruvic acid yielded similar results. The method selected was ingenious but did not lead to the desired end.

2. In the same year (1901) Kipping attempted to solve the problem by a method similar to that used by Cohen and Whitely. Benzoyl-formic acid was changed into an active ester by heating with borneol. The resulting ester was then reduced, whereby the carbon atom of the carbonyl group was rendered asymmetric. By hydrolysis the active bornyl radical (Byl) was removed,

leaving an acid which contained the newly synthesized asymmetric group:

$$C_6H_5COCOOH \rightarrow C_6H_5COCOOByl \rightarrow C_6H_5\overset{*}{C}HOH$$
$$COOByl \rightarrow C_6H_5\overset{*}{C}HOHCOOH.$$
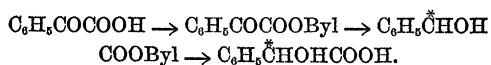
The results however were negative, the mandelic acid formed being inactive.

Kipping also attempted to effect a partial asymmetric synthesis through the influence of an optically active solvent. For this purpose he prepared benzoin through the action of potassium cyanide upon benzaldehyde in an alcoholic solution of camphor:

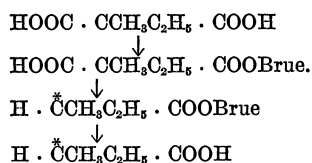$$2 C_6H_5CHO \rightarrow C_6H_5\overset{*}{C}HOHCOC_6H_5.$$

He likewise synthesized mandelic acid nitrile by the action of hydrocyanic acid upon benzaldehyde in an alcoholic solution of camphor; pyruvic acid and methylethylketone were reduced in a concentrated solution of grape sugar. While all of these reactions led to the synthesis of compounds containing an asymmetric group, the products in each case were inactive, showing that the two forms had been synthesized in equal quantities.

3. Two years later (1902–03) Fischer and Slimmer made another unsuccessful attempt to effect a partial asymmetric synthesis, using the optically active aldehyde, helicin, which is readily obtained from natural sources, as the active constituent for influencing the synthesis. The aldehyde group was rendered asymmetric by the addition of hydrocyanic acid as well as by the action of zinc ethyl. The resulting compounds were decomposed so that one of the products formed contained the newly synthesized asymmetric group. The products, however, proved to be inactive.

4. The first successful attempt to effect a partial asymmetric synthesis was made by Marckwald in 1904. In this investigation, brucine was used as the active agent. Marckwald started with methylethylmalonic acid. This was converted into the brucine

salt. Upon heating this salt carbon dioxide was split off, rendering the central carbon atom asymmetric. The resulting salt was treated with an acid, liberating the free methylethylacetic acid:

$$HOOC . CCH_3C_2H_5 . COOH$$
$$HOOC . CC\overset{\downarrow}{H_3}C_2H_5 . COOBrue.$$
$$H . \overset{*}{C}CH_3C_2H_5 \overset{\downarrow}{.} COOBrue$$
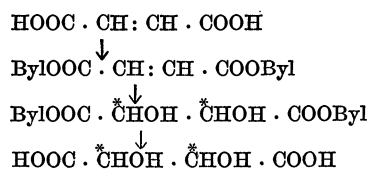$$H . \overset{*}{C}CH_3C_2H_5 \overset{\downarrow}{.} COOH$$

This product was found to be slightly levo-rotatory. The results showed that while both the dextro and levo forms of the acid had been produced, there was an excess of about 16 per cent. of the levo form.

5. Following Marckwald, MacKenzie and his co-workers carried on a series of investigations in 1904, 1905, 1906, 1907, and in 1909, in which they were able to effect a number of partial asymmetric syntheses. The principal method employed by MacKenzie was very similar to that used by Kipping. An acid of the general formula R-CO-COOH was selected and changed into an optically active ester by combination with an active alcohol, such as amyl alcohol, borneol or menthol. The carbon atom of the carbonyl group was then rendered asymmetric by the action of Grignard's reagent as well as by reduction.

The resulting products, freed from the active alcohol groups, proved to be slightly active, showing that a partial asymmetric synthesis had been accomplished. A comparison of the results obtained by the use of amyl alcohol, borneol and menthol led to the conclusion that the greater the optical activity of the influencing group present, the greater is the extent of the asymmetric synthesis.

MacKenzie was also able to synthesize both dextro and levo tartaric acids in an ingenious way (1907). Fumaric acid was changed into the active bornyl or menthyl ester and this ester was then oxidized by potassium permanganate. The two central carbon atoms were thereby rendered asymmetric:

$$HOOC . CH : CH . COOH$$
$$\overset{\downarrow}{BylOOC} . CH : CH . COOByl$$
$$BylOOC . \overset{*}{C}\overset{\downarrow}{H}OH . \overset{*}{C}HOH . COOByl$$
$$HOOC . \overset{*}{C}H\overset{\downarrow}{O}H . \overset{*}{C}HOH . COOH$$

On saponification the resulting product yielded an optically active mixture of tartaric acids, indicating an excess of either the dextro or levo form. When menthol was used as the active agent the levo acid was in excess; when borneol was used, an excess of the dextro acid was obtained.

6. Mention should be made of the attempts to effect the synthesis of compounds containing asymmetric groups other than those of carbon. Smiles, in 1905, effected the synthesis of compounds containing asymmetric sulfur groups while E. and O. Wedekind, in 1908, built up asymmetric nitrogen groups. In neither case, however, were partial asymmetric syntheses effected. The method employed by E. and O. Wedekind was similar to that employed by Kipping in that the reactions were carried out in an optically active solvent such as *l*-menthol and *d*-limonene.

7. A distinct advance in our knowledge of asymmetric syntheses was made by Rosenthaler in 1908. Recalling the discovery of Pasteur that certain enzymes have a different action upon the dextro and levo forms of some of the sugars, Rosenthaler attempted an asymmetric synthesis by the addition of hydrocyanic acid to benzaldehyde in the presence of emulsin. By hydrolyzing the resulting compound pure levo-mandelic acid was obtained. Rosenthaler's results are especially significant; for while all the other attempts to effect partial asymmetric syntheses yielded both active forms, but with the one in slight excess of the other, Rosenthaler obtained

the one form only. It may be, however, that the reactions which Rosenthaler employed gave rise to both forms and that the dextro form was destroyed as fast as it was synthesized, through the action of the emulsin.

8. The most important contribution to the subject of asymmetric syntheses in recent years is that made by Bredig and Fiske in 1912. Bredig and Fajans had previously shown that the dextro and levo camphor-carboxylic acids decompose with different speeds in the presence of active bases. When the reaction is carried out in nicotine solution, for example, the speed of decomposition of the *d*-acid is about 13 per cent. greater than that of the *l*-acid—results that are similar to those of Dakin, who studied the hydrolysis of mandelic esters in the presence of lipase. With this information concerning the selective action of the alkaloids in mind, Bredig and Fiske attempted to utilize this property of alkaloids in effecting asymmetric syntheses. For this purpose they selected the same reaction that Rosenthaler had used, namely, the addition of hydrocyanic acid to benzaldehyde, but substituted an alkaloid for the emulsin. The results were decisive. In the presence of quinine an excess of dextro mandelic acid was formed, while quinidine gave an excess of the corresponding levo compound. The alkaloid acted as a catalytic agent since the results were obtained by the use of relatively small amounts of the bases.

While all the methods for effecting partial asymmetric syntheses so far discussed differ somewhat in detail, yet they are all fundamentally the same. In each case the object has been to bring about an asymmetric synthesis through the agency of the forces exerted by a previously existing asymmetric group. Now it is perfectly rational to suppose that in place of the forces exerted by an asymmetric group, one might utilize the forces acting in a strong magnetic field or those exerted in either plane or circularly polarized light. Accordingly, many attempts have been made to employ these agencies. Pasteur himself used the magnetic field as the active agent, as did also Boyd (1896). Meyer, in 1903, believing that the forces exerted in a magnetic field are not of the same character as those exerted by an asymmetric group, attempted to improve the experiment through the combined influence of a magnetic field and polarized light. Henle and Haakh (1908) concluded that a reaction that proceeds in the absence of light is not likely to be influenced by the action of polarized light. Accordingly they attempted to effect an asymmetric synthesis by the decomposition of certain acids of the type of malonic acid, through the action of light in the presence of uranium compounds—a reaction which will take place under the conditions of the experiment, only in the presence of light. In all of these investigations, however, no positive results were obtained.

The results of all the attempts to effect either a partial or complete asymmetric synthesis may be summed up as follows: in so far as we are able to detect with instruments at present constructed, an asymmetric compound synthesized from its constituent elements or from optically inactive compounds is always obtained in the inactive form. The optically active forms can be prepared synthetically only through the assistance of previously existing optically active compounds.

In making this general statement I am disregarding the work of Stoklosa and his co-workers (1913), who claim to have prepared optically active sugars through the action of ultra-violet light upon a mixture of carbon dioxide and hydrogen in the presence of potassium hydrogen carbonate. Stoklosa's results are of the greatest im-

portance if true, but serious doubts have been cast upon their accuracy so that they have not been at all generally accepted.

WILLIAM McPHERSON
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(*To be concluded*)

THE COMMITTEE OF ONE HUNDRED ON SCIENTIFIC RESEARCH OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

THE committee held its fourth meeting at the Hotel Belmont, New York City, convening shortly after two o'clock on the afternoon of December 26, 1916. Mr. Pickering was in the chair and others recorded as present were:

Raymond F. Bacon, Franz Boas, N. L. Britton, Alfred H. Brooks, Ernest W. Brown, Walter B. Cannon, J. J. Carty, J. McK. Cattell, C. R. Cross, Chas. B. Davenport, W. M. Davis, Henry H. Donaldson, H. L. Fairchild, Irving Hardesty, G. Ross Harrison, L. O. Howard, Aleš Hrdlička, W. J. Humphreys, Edward Kasner, A. E. Kennelly, Irving Langmuir, Berthold Laufer, Frederic S. Lee, Jacques Loeb, D. T. MacDougal, J. C. Merriam, G. A. Miller, T. H. Morgan, H. V. Neal, Edw. L. Nichols, A. A. Noyes, Richard M. Pearce, M. I. Pupin, Jos. W. Richards, F. K. Richtmyer, Peyton Rous, H. N. Russell, Frank Schlesinger, Geo. Otis Smith, J. Stieglitz, Chas. R. Stockard, E. L. Thorndike, A. M. Tozzer, Charles R. Van Hise, John B. Watson, A. G. Webster, David White, W. R. Whitney, Edmund B. Wilson, W. M. Wheeler, R. M. Yerkes.

After introductory remarks by the chairman, the secretary reported that, since the organization of the committee at Atlanta four years ago, it had lost by death: Charles E. Bessey, professor of botany, University of Nebraska; Theodore Gill, professor of zoology, George Washington University; Karl E. Guthe, professor of physics, University of Michigan; Joseph A. Holmes, chief of the Bureau of Mines, Washington, D. C.; Charles S. Minot, professor of comparative anatomy, Harvard Medical School, and F. W. Putnam, professor emeritus of anthropology, Harvard University. There had been added to the committee: Raymond F. Bacon, director of the Mellon Institute for Industrial Research, the University of Pittsburgh; W. B. Cannon, professor of physiology, Harvard Medical School, and John C. Merriam, professor of paleontology, the University of California.

Since the meeting last year at Columbus the following subcommittees in different sciences had been appointed:

Mathematics: G. A. Miller, *Chairman*, Edward Kasner, E. H. Moore, W. F. Osgood, E. B. Van Vleck.

Astronomy: Edward C. Pickering, *Chairman*, E. W. Brown, E. B. Frost, H. N. Russell, F. Schlesinger.

Physics: Arthur G. Webster, *Chairman*, C. E. Mendenhall, Ernest Merritt, R. A. Millikan, M. I. Pupin.

Chemistry: Julius Stieglitz, *Chairman*, I. Langmuir, G. N. Lewis, W. A. Noyes, T. W. Richards.

Engineering: A. E. Kennelly, *Chairman*, J. W. Richards, A. Sauveur, A. N. Talbot, C. C. Thomas.

Geology and Geography: Wm. M. Davis, *Chairman*, Alfred H. Brooks, L. C. Glenn, C. K. Leith, Bailey Willis.

Botany: George T. Moore, *Chairman*, D. H. Campbell, R. A. Harper, L. R. Jones, B. E. Livingston.

Zoology: Edwin G. Conklin, *Chairman*, F. R. Lillie, T. H. Morgan, G. H. Parker, Jacob Reighard.

Anatomy: Ross G. Harrison, *Chairman*, F. P. Mall, C. R. Stockard, C. M. Jackson, Irving Hardesty.

Pathology: Richard M. Pearce, *Chairman*, Theodore C. Janeway, Eugene L. Opie, Peyton Rous, H. Gideon Wells.

Physiology: W. B. Cannon, *Chairman*, Joseph Erlanger, Theodore Hough, Frederic S. Lee, Walter J. Meek.

Psychology: J. McKeen Cattell, *Chairman*, C. E. Seashore, E. L. Thorndike, John B. Watson, Robert M. Yerkes.

Anthropology: Franz Boas, *Chairman*, A. Hrdlička, Alfred L. Kroeber, Berthold Laufer, Alfred M. Tozzer.

Reports were presented by the chairmen of nearly all the subcommittees. The report of the subcommittee on industrial research, presented by Mr. Bacon, was a special order, and by invitation was discussed by Mr. J. J. Carty, chairman of a committee of similar scope of the National Research Council and by Mr. F. K. Richtmyer, secretary of a corresponding committee of the American Physical Society.