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Alicyclic compounds

Nobel Lecture, December 12, 1910

The extraordinary honour of being allowed to address this illustrious assembly and to express my thanks for the superb recognition bestowed on my modest work by the Royal Swedish Academy of Sciences, gives me a feeling of happy pride at having been found worthy of distinction by such a distinguished body of men. But I am also deeply moved by another emotion. This place, where Jacob Berzelius once worked is, from the scientific point of view, a holy land for chemists, where, on entering, one still seems to sense the presence of this reverence-inspiring immortal genius. Berzelius sowed the seed, the fruit of which we are reaping now. It is no mere accident, but a logical historical evolution that Friedrich Wöhler concluded his studies here in *Stockholm*, which enabled him to carry out his pioneering work on the essential oil of bitter almonds in *Göttingen*, and that today Wöhler's pupil and successor to the professorial chair in Göttingen has been invited to report on the progress achieved during the recent decades in the field of "cyclic compounds", among which many components of essential oils must be counted.

The chapter of organic chemistry which I shall discuss first, really belongs to that field which Berzelius had included under the heading of "vegetable chemistry".

From a very early age onwards people's attention had been attracted to the volatile substances, characterized by strong smells or flavours, which are among the large variety of substances which form within plants; these were used partly for therapeutic purposes, but in particular for increasing pleasurable sensations by nerve stimulation. Food was flavoured with fragrant herbs; eminent persons whom one wanted to honour, were anointed with exquisite oils; the air in places where acts of worship were performed, was saturated with incense, gum benzoin and myrrh and other scented narcotic drugs; and even the dead were enveloped in fragrant substances before burial.

In consequence of their wide application, spices and seasonings became important trading articles early in history. Trading caravans and later on the

proud ships of the maritime nations dominating the seas, brought even in earliest times to the West and to the northern countries less favoured by Nature, where cinnamon, vanilla, cloves, cardamon and camphor cannot thrive, these precious *aromata*, from the blessed fields of the Orient, where even today there is a strong predilection for high-flavoured spices and heavily scented substances.

Initially only the drugs themselves were used, but later people learnt to extract from the fragrant plants their essential components, the essences, just as they learnt how to produce spirit of wine from the fruit of the vine, and, so to speak, present them in a more concentrated form. This is the start of the history of essential oils.

This is not the place to discuss the methods by which the volatile vegetable substances were obtained, whether by simple heating (so-called dry distillation) or by distillation with steam, or by extraction; neither is it possible to discuss how each of these methods was gradually improved until the present degree of perfection was reached, above all by fractionation of the substances in a vacuum or under reduced air pressure instead of under normal atmospheric pressure; these methods made distillation easier and prevented the formation of undesirable decomposition products during the process.

With time the number of known volatile vegetable substances has increased considerably. It has been possible to trace historically back to a very early age the taxes which were imposed on medicines, spices and similar substances in German towns. Thus, for instance, one finds that in the year 1500 thirteen, in 1540 thirty-eight and in 1708 already one hundred and twenty vegetable oils are mentioned. Nowadays their number is many times larger.

In vast modern factories engaged in extracting essential oils, of which the firm Schimmel & Co. in Miltitz near Leipzig is one of the most important, any kind of plant containing these oils is systematically processed, if obtainable in large enough quantities, and the oils are extracted for a detailed investigation of their components.

The scientific study of the components of the vegetable oils, however, has only been undertaken in modern times. Initially, nobody knew what to do with them from a chemical point of view. The investigation of the essential oil of bitter almonds, undertaken jointly, as already mentioned, by Wöhler and Liebig in 1832 was of epoch-making importance. These famous chemists proved that bitter almonds contain, besides liquid and non-volatile fatty oil, an inodorous solid substance, namely amygdalin, which, under the influence

of acids or ferments absorbs water and splits into glucose, prussic acid and the volatile, strong smelling bitter almond oil. From the series of ferments or enzymes, as called nowadays, which initiate the splitting, one is contained in the almond itself, namely the emulsin. The smell of bitter almonds becomes noticeable as the emulsin causes this splitting reaction. Such substances causing chemical reactions by their mere presence are called catalysts, following Berzelius' proposal. The process itself is called catalysis. In recent times the catalytic phenomena have again been in the foreground of theoretical and practical chemical interests. In this connection it is therefore important to mention briefly the observations made on amygdalin by Wöhler and Liebig, because these illustrate by which processes volatile, odorous substances can form from non-volatile, odourless matter in plants. Substances which have the ability of splitting into more simple volatile ones etc. in the presence of vegetable ferments, are those with a more complex composition. We shall refer to this again later on.

In the first instance we are interested in bitter almond oil itself, this fragrant main component of an important essential oil.

The investigation of this substance by Wöhler and Liebig is regarded as one of the most classic and memorable in chemical science. It showed for the first time that in organic as well as in inorganic compounds, certain compound radicals could play the part of simple substances. This was, in Berzelius' formulation, the sign of a new dawn breaking with regard to organic chemistry. And yet, almost another generation had to go by before the dawn gave way to the full light and the structure of "*benxoyl*", the chemical radical contained in bitter almond oil, became quite clear. Only in 1865 did the ingenious conception of Kekulé find the solution to the up till then mysterious nature of the "aromatic substances", to which bitter almond oil belongs. In bitter almond oil, like in a great number of other substances that previously had been counted among the "aromatic compounds" on behalf of their strong smell, a derivative of benzene is present. The special properties of benzene and its derivatives are caused by the typical arrangement of their carbon atoms. Kekulé demonstrated that the arrangement of the atoms in the normal organic compounds is chain-like, whereas in benzene and its derivatives it is in the form of rings. It is precisely the substances appertaining to the latter group which are distinguished by characteristic smells, particularly those belonging to the aldehydic type of compounds. Bitter almond oil proved to be nothing other than the simplest aldehyde of the benzene series, namely benzaldehyde.

Following this, it was not difficult to determine that substances, the structure of which is quite analogous, can cause the strong odour of vegetable matter; thus, e.g. cinnamic aldehyde causes the smell of cinnamon oil and cassia oil. Anisic aldehyde, vanillin, heliotropin are also aldehydes derived from benzene and occur in the well-known plants to which their names refer. Mention can also be made of substances appertaining to other types of compounds in the benzene series, which are vital components of strong-smelling plants. Among these are e.g. coumarin in *Asperula odorata* (woodruff), some of the phenols, such as thymol from the oil of thyme and in particular a large number of esters. For instance, it has been known for a long time that oil of winter green consists mainly of salicylic acid methyl ester. More recent research has shown that the ester of anthranilic acid, an acid containing nitrogen (*o*-aminobenzoic acid, $C_6H_4(NH_2)CO_2H$), plays a role in some strong-smelling oils.

But, however important the benzene compounds may have proved to be for the aromatic nature of many oils, it became apparent that such benzene derivatives could not be regarded as vital components of numerous other essential oils. In this connection mention must be made of the turpentine oils proper, the various oils extracted from the needles of Coniferae, orange-peel oil, caraway oil (carvone), peppermint oil, eucalyptus oil, fennel oil, thuja oil, camphor oil, and many others. Initially there was no explanation available on the nature of the substance occurring in this group of oils.

It was impossible to define these substances chemically, and the components which had been observed were at first divided into two groups according to their physical properties.

Compounds which are liquid like turpentine oil and remain in a liquid state even at low temperatures, were called "terpenes", and those that were solid, like camphor were called "camphors" Berzelius had already objected to the usage of designating all components of essential oils that precipitated in solid form as camphors, and proposed calling the liquid substances *elaeoptenes*, and the solid ones *stearoptenes*. In spite of the justified objections raised by Berzelius, who considered that the old designations were misleading, as many solid precipitations from oils have no connection whatsoever to camphor, this old distinction between terpenes and camphors has not disappeared. However, the latter designation was later only retained for oxygenous compounds with identical or similar composition as the ordinary camphor; the liquid compounds of such structure were also called camphors.

Various difficulties were encountered when a start was made on identifying

the chemical composition of the oils in question analytically, because in most cases one was dealing with mixtures of substances, difficult to separate from each other. However, very soon a characteristic fact became evident, namely that all important bodies appertaining to this group have 10 carbon atoms.

In organic chemistry we have learnt to derive from compounds containing only carbon and hydrogen, i.e. from the hydrocarbons, all other types of combinations, such as alcohols, aldehydes, ketones, acids, etc. Systematic scientific research therefore had to start with the terpene hydrocarbons. These, the terpenes proper, have 16 hydrogen atoms linked with 10 carbon atoms, therefore the chemical formula is $C_{10}H_{16}$.

Round about the middle of last century eminent French chemists (e.g. Berthelot and Riban), in particular, had already investigated these hydrocarbons. Of great importance in these investigations was the fact discovered by Biot round about 1816 that turpentine oil, camphor and related compounds could deflect a polarized beam of light. The direction and intensity of the deflection appeared to be characteristic properties of optically active bodies. Since active terpenes which showed larger or smaller divergences in their optical behaviour were found in a great variety of plants, these substances of different origins were regarded as being different from each other. Accordingly, they were given names derived from the starting material, such as terebenthene, camphene, citrene, carvene, cynene, cajeputene, eucalyptene, hesperidene and so on. Gradually in this way, a great number of terpene hydrocarbons were listed in the literature, and the matter became more and more confused and obscure.

It was improbable from the start that there should be so many different hydrocarbons $C_{10}H_{16}$ occurring naturally, as had been assumed and it was obvious that in many cases the divergences observed in the properties had been caused by the presence of impurities. But there were no means available for ascertaining this, because not enough chemical characteristics were known about either the terpenes or their derivatives.

It is true that as early as 1803 Kindt has produced a characteristic solid compound containing chlorine (the present pinene hydrochloride $C_{10}H_{17}Cl$) when he treated turpentine oil with hydrochloric acid; this compound, on account of its smell and the already discussed usage of designating solid precipitates from such oils, was simply called "synthetic camphor". A little later Thenard produced in the same manner another solid compound (the present dipentene dihydrochloride $C_{10}H_{18}Cl_2$) and very much later (1877) Dr. Albert Atterberg in Uppsala made the important discovery that another, easily

crystallizing compound (sylvestrene dihydrochloride) could be obtained from certain Swedish oils, and at about the same time Tilden discovered that some terpenes combine with nitrosyl chloride to form substances which are difficultly soluble. But all knowledge gained by the middle of the 1880's was not adequate to clear up these matters, all the more as the investigations were up against another difficulty: namely the fact that the terpenes are extraordinarily unstable substances. They resinify not only easily by absorbing oxygen when exposed to air, but to a certain extent also when stored for some time without air. This is manifested by the change in physical properties, boiling point, density, and optical behaviour. In particular, these substances suffer displacements in the structure of the molecule under the influence of chemical reagents without, however, changing their composition; *isomerizations*, as they are called in accordance with Berzelius' proposal, take place and this phenomenon is more pronounced in the terpenes than in any other previously known substances.

The premise for any successful investigation therefore was the task of determining definite and reliable distinguishing characteristics for those terpenes which really differ from each other.

Several useful new observations, among others those on crystallized bromination products of the hydrocarbons, have enabled me, by taking into account and further developing the reactions already known, to achieve this aim to such a degree that it is now possible to name sufficient distinguishing characteristics for the various substances within this group. It now became evident that the number of the known terpene hydrocarbons that differ from each other from a chemical point of view, is in fact quite small; at the same time it was possible to separate, facilitated by previous investigations, the existing modification into clearly defined main groups, according to density, boiling point and refractive power. After the accurate diagnosis on the presence of certain compounds had been ensured—even if they only appeared as a part constituent as in essential oils—it was possible to tackle the next task, namely the determination of the mutual chemical relations of the oxygenous and oxygen-free constituents of essential oils.

By suitably converting hydrocarbons into oxygenous compounds and, reciprocally, oxygenated substances into hydrocarbons, and by effectuating the transitions, it was practicable to find the connection between a very large number of substances occurring in essential oils and appertaining to the terpene group and to trace the genetic relationship between the various substances.

It would be hopeless to try and attempt to discuss within the short time available the long series of experiments that were successfully carried out with this purpose in mind. I have given a short tabular survey of my experiments on pages 38-51 of my book "*Terpene und Campher*" (Terpenes and Camphors).

Listing only a few examples here, I want to mention that I succeeded in converting the main component of the ordinary turpentine oil, namely pinene, $C_{10}H_{16}$, into the odiferous constituent of caraway oil, namely *carvone* $C_{10}H_{14}O$, and then reconverting this into the isomers of pinene, i.e. limonene and terpinene. It was possible to convert this same pinene via the lilac-scented alcohol terpineol to eucalyptole, $C_{10}H_{18}O$, the main constituent of worm-seed oil (chenopodium oil) and of the oil from *Eucalyptus globulus*, and to convert this in turn to *l*-limonene, and so on.

As already mentioned, the main purpose of these investigations was the attempt to find links between the various known compounds in order to gain understanding of their mutual relationships; among other factors, reduction of an unsaturated compound to one with a higher degree of saturation played an important part. For instance, the following series is known: $C_{10}H_{14}O$, *carvone*; $C_{10}H_{16}O$ dihydrocarvone; $C_{10}H_{18}O$ tetrahydrocarvone. It was a simple matter to convert the active *carvone* $C_{10}H_{14}O$ into dihydrocarvone by direct addition of hydrogen. The last step, however, to $C_{10}H_{18}O$ could not be accomplished directly by the normal chemical reduction methods. Dihydrocarvone does not continue to absorb nascent hydrogen produced by a chemical process.

This aim, therefore, could only be reached in a roundabout way. Dihydrocarvone was rearranged into an isomeric compound, namely *carvenone*. This then absorbed hydrogen and resulted in $C_{10}H_{18}O$. However, *carvenone* is no longer optically active and therefore neither is its reduction product. So, up to that time it had not been possible to obtain active tetrahydrocarvone directly from *carvone*. I am very happy, however, to be able to tell you that within the last few weeks I was able to eliminate conclusively this difficulty. I found, quite unexpectedly, that *carvone* can be reduced directly to active tetrahydrocarvone by allowing free hydrogen to act on *carvone* at normal temperatures and in the presence of colloidal palladium. This process can also be excellently applied to other compounds of our series, which otherwise would have been completely unaffected by direct reduction. It has made possible for certain cases the realization of transitions which had previously seemed impossible and represents a definite step forward. It is

particularly remarkable to note how much more effectively the molecular hydrogen reacts as compared with the nascent hydrogen, which so far has been regarded as being of far superior efficacy.

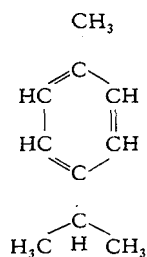
The investigations on the mutual relationships among the terpene compounds have been profitable in other directions as well.

As already mentioned, most of the terpenes are optically active substances. We know that the hypothesis of Le Bel and Van 't Hoff (1874) was the correct interpretation of the phenomenon of optical activity and that prior to this Pasteur had found when mixing equal quantities of laevo-rotatory and dextro-rotatory modifications of a substance in solution, a new substance with quite different properties may result. A mixture of laevo-tartaric acid and dextro-tartaric acid resulted in inactive meso-tartaric acid, the properties of which are entirely different from those of the active constituents. But up to the year 1888 this was the only experimentally established example of *racemization*, as this phenomenon was called (derived from the name *acidum racemicum* for tartaric acid).

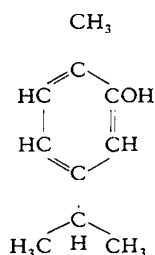
With the discovery of the occurrence of laevo-limonene in the needles of *Pinus sylvestris*, whereas so far only dextro-limonene had been known (as is found e.g. in the orange-peel oil) and with methods of producing well-crystallized derivatives of limonene at my disposal, I was now in a position to obtain whole series of racemic compounds from their active constituents; a secondary result was the discovery that the terpene hydrocarbon dipentene, which so far, on account of the peculiarity of its derivatives had been regarded as a special terpene, is nothing but inactive limonene.

The experiences which were gathered in investigating the mutual relationships between the terpene compounds also assisted in preparing the final solution of the question which is always the most important and most interesting one for theoretical chemists, namely what the internal structure of the molecule, or the constitution, as chemists call it, of this group of compounds would be.

All recent experiments had already confirmed the accuracy of an older assumption, namely that the hydrocarbons $C_{10}H_{16}$ occurring naturally, are related to a benzene hydrocarbon $C_{10}H_{14}$, the so-called *cymol* (isopropyl-*p*-methylbenzene):



Pinene, camphor and other compounds can be converted by appropriate chemical processes to cymol or cymol derivatives, e.g. *carvacrol*:



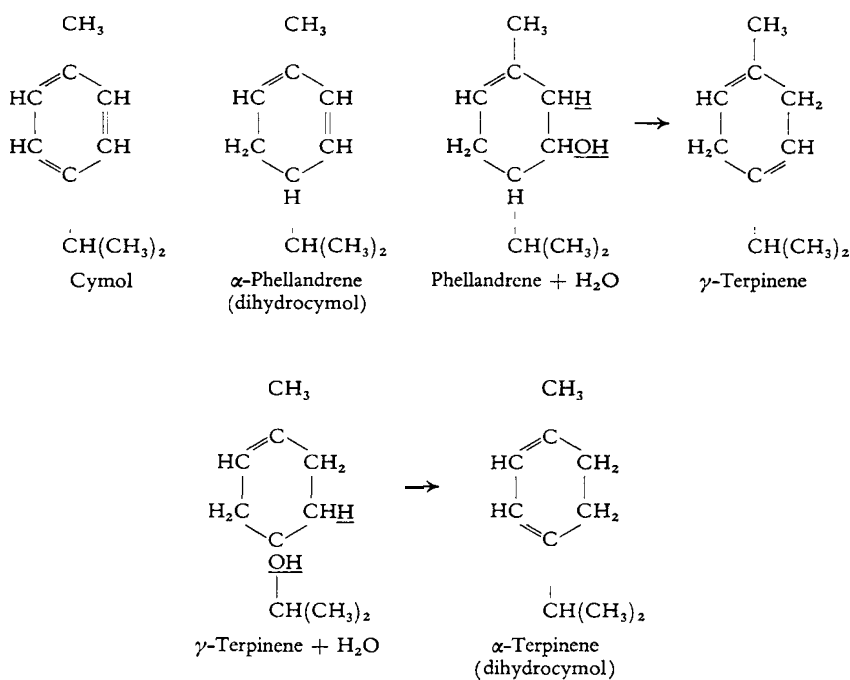
Kekulé, the brilliant originator of the benzene theory, had already expressed the opinion that terpenes were partially reduced cymol. He assumed in the benzene compounds - as shown by our formula - a nucleus of six carbon atoms, which carry, when cyclically linked, three so-called double bonds between the carbon atoms. If one then imagines, for example, one of these double bonds converted into a single bond by the addition of two hydrogen atoms, one arrives from $\text{C}_{10}\text{H}_{14}$ at $\text{C}_{10}\text{H}_{16}$, i.e. a substance with terpene composition. When Kekulé advanced this opinion, the practicability of dissolving bonds in benzene by absorption of hydrogen was only a hypothesis. The credit for proving by experiments that such an additive process is really feasible must essentially go to Ad. von Baeyer, who proved that by doing so, substances could be obtained which have lost their characteristics of benzene compounds, although they still have a ring-like or cyclic (as it is now usually called) arrangement of atoms, and rather resemble in their behaviour the ordinary or aliphatic combinations with chain-like pattern of atoms. Later the designation *alicyclic* was introduced for such compounds (also for other cyclic systems).

In accordance with this concept therefore the terpenes would appear to be

a special case of alicyclic compounds, which form by accident - or for reasons which we as yet do not understand-with particular ease in plants.

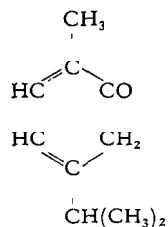
In the main this concept has proved to be correct, even if not quite adequate, as we shall now see. It explains, among other things, why terpene compounds isomerize with such ease (i.e. displace the bonds contained in them). Unsaturated substances (i.e. in our view those containing carbon double bonds) can be added to and can absorb e.g. water, acids, etc. by dissolving existing bonds. The added components can then, in certain circumstances, be split off in directions different from those in which they had been picked up. Thus we arrive at so-called bond displacements, i.e. isomerizations.

The following structural formulae give an example which makes the relation of *phellandrene* and *terpinenes* to *cymol* clear and explains the isomerizations which may occur when water is added and split off, respectively.



However, Kekulé's interpretation could not be used to explain the behaviour of some terpenes, in particular that of the most widely used one, which has been known longest, i. e. *pinene*, the main constituent of the French,

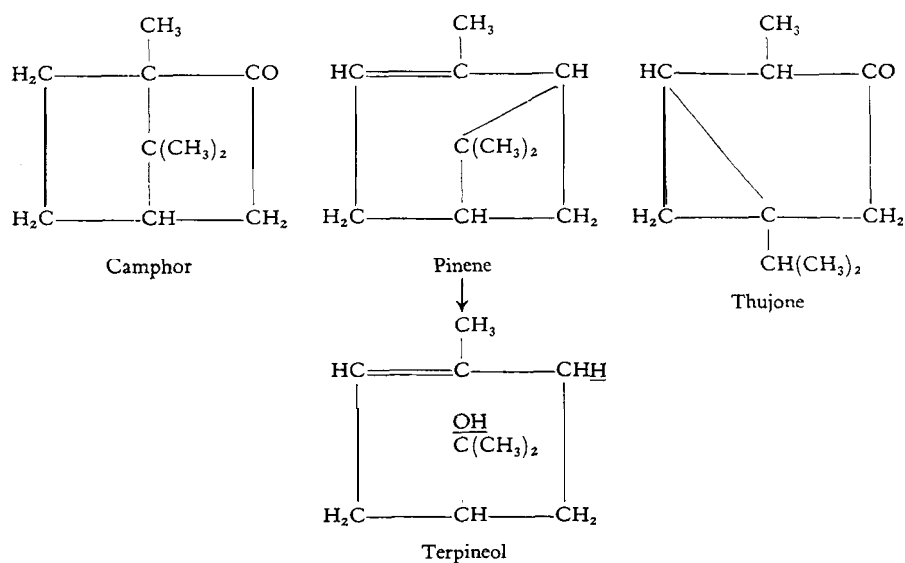
American and Swedish turpentine oil. The same applies to camphor, which Kekulé regarded as the ketone of dihydrogenated cymol, something like:



I must confine myself here to the brief statement that it has now been accepted with certainty that the substances mentioned, and also analogous ones, have their molecule constructed from two mutually interlaced carbon rings, in such a way that when one ring dissolves, the double-ring system again becomes a single one.

The simplest case of this kind occurs with the so-called diagonal bond in the molecule. Brecht proved by a series of excellent experimental investigations that camphor contains two intertwined five-ring compounds. In pinene a four-membered ring is combined with a six-membered one; thujone combines a three-membered ring with a five-membered one.

The following formulae will illustrate the prevailing concept and will also show how, e.g. the double-ring system of pinene can change into a single ring system by water absorption (conversion of pinene to terpineol) :



Credit is principally due to Semmler for having demonstrated that another quite different group of substances contained in essential oils, and distinguished by particular smells, does not belong to the cyclic compounds at all, but to the category of unsaturated aliphatic compounds. These, however, have a strong tendency towards ring formation, and therefore towards conversion to cyclic compounds. One of these substances for instance is citral, which imparts to the oil of lemons its lemon odour, and geraniol, which smells of roses.

As soon as chemists have a definite conception of the internal structure of the molecule of an organic compound, they are able to tackle the task of producing these substances by artificial methods, i.e. by synthesis, as we call it. As far as the terpene compounds occurring naturally were concerned, peculiar difficulties in connection with the synthesis had to be overcome even after their structure was known; these were mainly connected with the sensitivity of these substances to chemical reagents. However, even in this field synthetic preparation had made great progress in recent years. Numerous methods have been made known, first of all for producing alicyclic compounds of terpene-like character; here the chemist differentiates between lower or higher homologous terpene compounds, according to whether the carbon content is smaller or greater than in the natural representatives, which contain 10 carbon atoms. However, also true terpene compounds such as limonene, lately also sylvestrene, terpineol, menthol, camphor and others, have been synthesized from their elements. Among the chemists, to whom great credit is due in this connection, W. H. Perkin Jr. deserves special mention. In any case, one may well say today: there are no more insurmountable difficulties in this field. Even if many of the problems have not been solved as yet: the veil has been removed from the mysterious picture of the terpenes and camphors and there is now nothing which impedes further rapid progress!

Distinguished Audience! It is by no means easy to treat simply and briefly the special subject that I have to discuss, even when addressing specialists, on account of the difficult material. It is even more arduous to make these matters clear in the difficult language of organic chemistry to an audience, which, although so broadly educated, is none the less not expert. I must therefore beg your great indulgence for the topics I have just been expounding to you in terms as general as possible. The majority of the distinguished audience

will probably find the following easier to understand; I shall now discuss the reaction which this progress in our field has had on the development of the industry, which is engaged in the preparation and practical utilization of the essential oils and their components.

Until about 25 years ago, the manufacture of essential oils was purely a matter of trial and error. The plants which contained odiferous constituents were simply distilled and the distillate was put on the market. In view of the lack of knowledge regarding their chemical nature, these products were not always handled in the right way, and above all, the door was wide open for adulteration. There was no remedy for this, even if it was carried out with only moderate skill. A strongly scented oil, like for instance the precious rose absolute, could easily be greatly diluted by worthless additives and the consumer had no reliable means of checking at his disposal. Now all this has been changed greatly. Thanks to the clear characterization of the individual components of essential oils, we now have available adequate analytical methods, by which adulterations can be proved and protection given against it. Apart from the purely chemical methods, investigations relating to the physical properties of the substances, like boiling point, density, refractive index, rotatory power are of great importance in these tests; all these properties were determined with the greatest care in the course of the work on the terpene compounds.

A further progress is denoted by the fact that the importance of the individual components of the essential oils can be correctly assessed on the basis of the knowledge gained. Previously it was thought that the hydrocarbons were of special importance for the scent properties of an essential oil. Now the contrary is known, they are often regarded as useless ballast, which the plant produces together with the really valuable substances, and a start has been made on the production of "terpene-free essential oils", which naturally have a much higher commercial value and are more suitable for practical use.

The endeavours to determine which constituents really impart the specific and valuable properties to an essential oil have led to another result important for the estimation of perfumes. Most of the oils which are valued as scents are mixtures of substances; only the combined effect of these leads to the known result. And in this connection the unexpected fact became apparent that the especially pleasantly scented natural oils not seldom contained a very small quantity of extremely malodorous substances, which nevertheless influence the effect of the scent. These are decomposition products of vege-

table proteins and are closely related to those which are formed by the decomposition of animal proteins in the digestive process and which give such a repugnant smell to faeces. One of these substances is indole. This, for example, is a characteristic component of jasmine oil, as was proved by Dr. Albert Hesse in a brilliant investigation.

This and similar experiences which could only be achieved by the progress in scientific investigations, have been in particular applied to good use by that branch of industry which is engaged in the artificial composition of scents. The preparation of such artificial mixtures is of quite old standing, the best known example being Eau de Cologne, which was invented in 1725, and is a combination of neroli oil and other substances.

Nowadays, however, artificial flower oils - such as rose-blossom oil, jasmine-flower oil, orange-blossom oil - are produced in excellent qualities on a scientific basis; these are not at all, or only slightly, inferior to the natural oils, but are not so exorbitantly expensive; an idea of the price of the natural oils may be given by the calculation that a single kilogramme of essential violet-blossom oil would cost 80,000 Mark and would require 33,000 kilogrammes of blooms.

The clever utilization for practical purposes of scientific results is the only cause of a highly flourishing essential-oil industry in Germany, with the result that this northern country is now an important competitor in the production of perfumery to the climatically much more favoured Romanic countries (especially the South of France).

The present output of the German essential-oil and artificial-scent industry is estimated at 40-50 million Marks annually. According to their own information, the firm of Schimmel in Miltitz alone have a stock of material of an average value of 2 million Marks.

How closely linked this flourishing industry is with the scientific development is apparent from the fact that the total chemical industry in Germany, which, as is well known, has been constantly increasing, has only doubled its production value in the period from 1850-1895, whereas the essential-oil industry has quadrupled its output during the same period.

We may well expect a lot more practical successes in the utilization of the synthetic methods developed during the last few years. For, as we have seen, the natural terpene compounds are only a special case in the infinitely large group of alicyclic compounds. We are now able to prepare substances which are analogous to the ones that occur naturally and which are distinguished by their smell, and these will therefore have similar properties, because similarly

constructed molecules usually have a similar effect on our nervous system. We can now predict, with certain limitations, that synthetically producible compounds with a certain molecular structure will smell of peppermint, or camphor, or caraway seed or lilac, etc. As soon as we can wrest from Nature the secret of the internal structure of the compounds produced by her, chemical science can then even surpass Nature by producing compounds as variations of the natural ones, which the living cell is unable to construct. In such a manner the great progress was partly achieved by the dyestuff industry, who has now produced compounds of e.g. the indigo and alizarine groups, which cannot be found in Nature. In the same way the pharmaceutical industry is producing compounds which are related to atropine and cocaine, which possess the physiological effect of these remedies, but which have been usefully modified somewhat for certain purposes.

Thus, in our field, too, chemical variation will lead to practical results.

Complete success has already been achieved by the chemical synthesis with regard to the already mentioned artificial preparation of ordinary camphor; in the past we have had to rely almost entirely on the production of the island of Formosa and the goodwill of the Japanese. Even if for various reasons the artificial production of this important substance is not an economic proposition yet, the certainty of having developed methods for the production of synthetic camphor from turpentine oil will prevent the branches of industry which need camphor, like the celluloid industry, from having to face another emergency as was temporarily experienced during the Russo-Japanese War.

As soon as science has solved one problem, new ones arise. This is the essence of science and it applies, of course, also to the field of essential oils.

In principle we now know what the substances are which are produced by plants in the form of essential oils; we can also determine their presence by reliable reactions; we have an idea of their molecular structure, and we can even produce them artificially - an accomplishment which Berzelius still thought impossible for all times.

But behind all this there looms a vast new problem, in comparison to which the one already solved seems quite small: the problem, what kind of chemical processes in the plant organism cause the formation of essential oils. How can we explain their infinite variety?

One would think that plants belonging to the same genus would always produce identical or at least similar oils. But this is by no means so.

As an example let us look at the family of the *Eucalyptus* species, to which the "fever tree", *Eucalyptus globulus*, belongs which is planted so extensively in Italy. This plant contains in its leaves, fruit and other parts eucalyptole or cineole, which imparts the strong smell and which is an oxygenous compound $C_{10}H_{18}O$. On the other hand, another species, *Eucalyptus amygdalina* produces no eucalyptole, but the terpene $C_{10}H_{16}$, i.e. phellandrene, which is characterized particularly by its inconstancy. Yet another species, *Eucalyptus citriodora* contains citronellal, which smells of lemons. *Eucalyptus piperita*, however, supplies a peppermint-scented substance.

Thus, plants botanically closely related form quite different products, and vice versa, some not related at all, produce sometimes identical substances. For instance, eucalyptole is produced just as abundantly from a composita, namely *Artemisia cinsae*, as from *Eucalyptus globulus*. Where is the connection? This can only be found out by a detailed investigation on the manner in which the essential oils in plants are produced and stored. We already know that many plants deposit these substances in special oil cells. This applies, e.g. to the oil in orange peel and orange blossoms. Therefore, these substances can easily be extracted from the plant parts by distillation with vapour. But this by no means applies to all cases. The fresh blooms of jasmine and tuberoses contain only very little oil, and distillation with vapour supplies only very small quantities of unpleasantly smelling substances. Odiferous substances, however, continue to develop in these plants, when the blooms have been cut and the plant begins to die.

Therefore, in these cases the valuable aromata are obtained by a quite different process as used for the preparation of, say, the orange peel or orange blossom oil, namely by the process of the so-called *enfleurage*. The cut plants are enclosed in a so-called "chassis", i.e. cases equipped with sheets of glass which have been covered with grease. The volatile substances which continue to form during that time are absorbed by the grease and can then be extracted from these fragrant pomades.

The processes which take place during this slow formation of odiferous substances in plants such as tuberoses, which can be closely watched, remind us of the facts which we learnt about the formation of the bitter-almond oil from the non-odorous amygdalin. Under the influence of fermentation, complex compounds are gradually split by delivering up the volatile constituents. But to find out what these complex molecules are and under what conditions they are formed must be the subject of further investigations.

We know that the production of essential oil in the plant is connected on

the one hand with its vegetative state, and with the cultivation conditions and other factors on the other hand. In recent times the French research scientist Charabot, in particular, has set himself the task of investigating this subject and these studies will bring us nearer to the solution of the question which substances should really be regarded as the parent substances for the production of the terpenes and camphors in plants.

Distinguished Audience! Theoretically and practically we have made great strides forward within the last quarter of a century in the field of which I have had the honour of giving you a short survey. But we still see in front of us a large fertile field which is waiting to be cultivated. The magnanimous Founder, whose memory we are honouring these days, in accordance with his high-minded intentions to foster science, wished to give recognition to scientific work that had been accomplished, but at the same time he wanted to inspire us to undertake new work. May the work for the further development of chemical science, which has its strongest roots in this beautiful, strong and hard-working country of Sweden, continue to flourish in the future, for the promotion of culture and the benefit of mankind.