

A SURVEY OF THE CHEMISTRY OF FREE RADICALS*

MOSES GOMBERG, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICHIGAN

In this short paper an attempt is made to give an historical outline of the rôle which the concept of radicals has played in the development of organic chemistry; this is followed by a brief survey of the class of compounds of recent origin known as triarylmethyls and related substances. These substances are all characterized by the presence in their molecules of one carbon atom which functions only through three valencies; its fourth valence remains dormant. In modern language, its fourth valence electron is neither shared with, nor transferred to, any other neighboring atom. In terms of older language these substances are the long-sought-for free radicals.

Lavoisier's Radicals

In accordance with his conception of the rôle played by oxygen, Lavoisier came to consider all mineral substances as oxygen compounds—metals on oxidation becoming bases and non-metals, acids. The primordial stuff which thus can give rise to base or acid, as the case may be, Lavoisier designated as the “radical” of the corresponding oxygen compound. At that time (1785) about twenty-five such radicals—our present-day elements—were already known to be actually capable of existence in the free state, *i. e.*, uncombined with oxygen or any other substance. Oxygen was thus set aside in this classification as a universal agent that could combine with all other elements. Lavoisier also determined the products of combustion of some organic substances, of alcohol, olive oil, tallow, and certain fruit acids. “I have observed,” he said, “that in the mineral kingdom all oxidizable radicals were simple; that in the vegetable kingdom, on the contrary, and above all in the animal kingdom, there were scarcely any radicals which were composed of less than two substances, hydrogen and carbon; that often nitrogen and phosphorus were also present; in this manner radicals were produced consisting of four components.”

This alluring idea of Lavoisier’s, that compound radicals in products of animate origin function parallel with simple radicals in substances of inanimate origin, remained dormant for almost thirty years.

Gay-Lussac’s Cyanogen Radical

By the middle of the second decade of the nineteenth century, the methods of elementary organic analysis were perfected to a considerable extent, and this made possible the classic investigation by Gay-Lussac

* Lecture delivered on the A. R. L. Dohme Foundation, at The Johns Hopkins University, April 27, 1930.

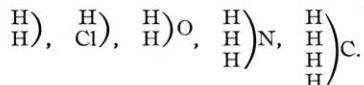
(1815) on hydrocyanic acid. Introducing for the first time the use of CuO as the oxidizing agent in combustion, Gay-Lussac determined definitely the composition of anhydrous prussic acid as being HCN; he prepared a number of salts and other derivatives of this acid. Finally, by heating dry mercury cyanide he obtained the cyanogen gas itself. Analysis showed the gas to have the composition (CN). Impressed by the fact that the group (CN) is retained unaltered in all the various derivatives, hydrocyanic acid, cyanic acid, salts of both acids, cyanogen chloride, etc., Gay-Lussac concluded: "This gas . . . presents a remarkable and, as yet, the unique instance of a substance which, although compound, none the less functions as a simple substance in its combination with hydrogen or with metals." Guided partly by these results of Gay-Lussac, and in part by his own findings concerning the compositions of organic substances, Berzelius could now well say, "In inorganic nature all oxidized bodies contain a *simple radical*, while all organic substances are oxides of *compound radicals*. The radicals of vegetable substances consist generally of carbon and hydrogen, and those of animal substances of carbon, hydrogen, and nitrogen."

Hypothetical Radicals

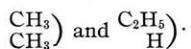
Henceforth, the theory of compound radicals, in one form or another, assumed a dominant influence in the development of organic chemistry. Through the whole period, from Gay-Lussac to Kekulé, the compound radicals continued to be merely hypothetical, and not real substances, with the exception of the three or four doubtful cases: Bunsen's cacodyl (1838-40), Frankland's and Kolbe's methyl, ethyl, and valyl (1840-50). And yet Dumas, Berzelius, Liebig, Bunsen, Frankland, Kolbe, and others kept reiterating their convictions that the actual isolation of the radicals in the free state was only a matter of time.

During the interval of the forty-five years, 1815-60, the concept of radicals and the implication of their function underwent a succession of deep changes. We may indicate four important periods. At first (1815-35) the radicals served primarily as agencies for classifying the ever-increasing number of organic substances. Around each radical, or what was surmised to be the true radical, was grouped a number of substances, heterogeneous yet related to each other by the fact of their being transformable, by appropriate chemical reactions, one into another, and all containing the same radical. The chemical properties of one group of substances differed from those of another, because of the difference in composition of the respective radicals in each of these two groups. Then followed a second period (1835-50) when the arbitrariness and the inadequacy of this system of classification were becoming apparent. It was being realized more and more that the analogy between simple radicals, elements, and the compound radicals is, at best, merely formal; the former

are immutable, the latter changeable by chemical means. Even more important than the circumstance of their mutability was the establishment of the fact that a deep-seated change in the composition of a compound radical did not always bring about a corresponding change in the chemical character of the new substances. To mention the most striking and most frequently quoted example, acetic acid, $(C_2H_3 \cdot O)_2O \cdot H_2O$, could be converted into trichloracetic acid, $(C_2Cl_3 \cdot O)_2O \cdot H_2O$, and yet there was but little difference in the chemical properties of the original and the new acid. The conclusion seemed inevitable that more important even than the *composition* of the radical is the rôle this radical plays in the structure of the compound. The composition of the radical may be changed, but if no appreciable alteration in the chemical properties of the compound had resulted from that change, then one is forced to infer that the general *type* of the original molecule has still been retained. If this inference be correct, then, vice versa, it was concluded that sameness of molecular type in structure should cause similarity of properties in the substances. But what could be the various possible types of structure? The answer to this question took shape within the next few years, 1848–58, thanks largely to the labors of Wurtz, Hofmann, Williamson, Dumas, and Gerhardt. The type theory came into being. This constitutes the third important change in the theory of radicals. According to this new doctrine, all organic compounds fall into five simple types, wherein the organic radicals replace the hydrogen in one or the other of five simple molecules:



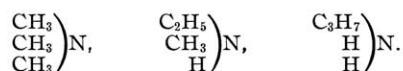
It matters little, so it was assumed, what the composition of the radical may be which replaces the atoms of hydrogen, so long as the *type* of the resulting molecule remains unchanged. The emphasis of classification was thus shifted to new ground. Instead of grouping a number of *heterogeneous* substances around one and the same radical as the pivot, it now became customary to group a large number of *analogous* substances around one and the same *type*, notwithstanding the fact that these substances may each contain different radicals in the molecule. The type became the all-important factor. On that new basis, homologous series of hydrocarbons, alcohols, aldehydes, and acids came into general use and existence of such series was readily explainable. It should not be a matter of surprise to us that Frankland, Kolbe, and other eminent men of that period saw possibilities of isomerism in the hydrocarbon C_2H_6 —namely:



Both structures were of the type of the hydrogen molecule, but one with only one radical, the other with two, and the two substances, so it seemed at that time, should differ in physical and chemical properties.

Valence Theory

Even the type theory of structure, however, failed to explain some of the difficulties that were being encountered. For instance, the existence of three isomeric amines, C_3H_9N , could be predicted on the type theory:



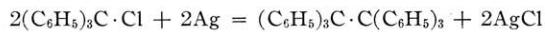
But in reality, four isomers existed, the fourth one having apparently the very same type structure as the third isomer. The conclusion was inevitable that even a radical itself may exist in isomeric forms. The time had arrived when it became necessary to assign an internal structure even to radicals themselves. It is in reply to this demand that our present constitutional formulas have arisen. The ground had already been prepared. The definite combining capacity, or valence, of various elements, N, P, Al, etc.—was recognized (Frankland, 1852), and when Kekulé perceived that the carbon atom itself may be considered as quadrivalent, the rationalization of the structure of organic compounds, down to the individual atoms, became possible. On the basis of the valence theory the radical, as something independent of the rest of the molecule, became an inconsistency. Isomerism of radicals became explainable on the basis of internal structure differences or atomic linking. This viewpoint constitutes the fourth important period in the changing concept as to the function of radicals in the structure of molecules. As time went on and the experimental evidence kept lending greater and greater support to the notion of quadrivalence in carbon, the less probable it appeared that exceptions, with carbon in valence of 3 or of 2, would be discovered. Ultimately, after the introduction of the periodic table (1870), the expectation of such exceptional cases was entirely given up. Even the previously reputed few exceptions—the radicals cyanogen, cacodyl, methyl, ethyl—on re-examination were found to be only apparent and not true radicals. All were found to have a molecular formula double that previously attributed to them; consequently they were not free radicals at all, and presented in their structure no exception to the doctrine of quadrivalent carbon.

Triarylmethyls

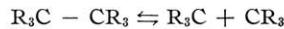
For full forty years, from 1860 until 1900, the valence hypothesis continued to serve as the one reliable guide in the phenomenal development of

organic chemistry, the constancy of quadrivalence of carbon serving as the basis of this whole development. The firmness with which the notion of fixed quadrivalence of carbon was entrenched by the end of the nineteenth century can be seen from the attitude as expressed at that period by Wilhelm Ostwald. In speaking of the Daniell cell and the unsuccessful attempts by Daniell to obtain the free sulfate ion, Ostwald, in his "Electrochemistry," published in 1896, makes this statement: "It took a long time before it was finally recognized that the very nature of the organic radicals is, inherently, such as to preclude the possibility of isolating them. And now it is becoming evident that the same holds true of ions."

It was against this background of uninterrupted progress for almost half a century that a publication appeared in 1900 with the title, "Triphenylmethyl, an Instance of Trivalent Carbon." The original intention of the experimenter was to prepare hexaphenyl-ethane, a saturated and presumably an entirely stable hydrocarbon. The experiment was carried out in conformity with well-tried and well-established procedure. The reaction anticipated may be expressed by the following equation:



Moreover, in view of the presumptive structure of the new compound, one was justified in predicting the properties that might characterize it. At first, the results were very erratic, but when the operations were carried out in an atmosphere of carbon dioxide, nitrogen, or hydrogen, they were reproducible. The resulting substance, however, possessed not one of the predicted characteristics. Instead of being colorless, the substance proved to be colored, at least when in solution; instead of being stable and inert, it was the very opposite—it combined with the oxygen of the atmosphere with an avidity reminding one of the reaction between yellow phosphorus and oxygen. Instead of being, as a saturated hydrocarbon should be, unresponsive to the action of iodine, it greedily united with it. In the presence of platinum it absorbed hydrogen. It was affected by merest traces of acids; decomposed by light. It conducted the electric current in ionizing solvents, such as liquid SO_2 , HCN . In brief, it showed characteristics which singled it out from all known classes of organic hydrocarbons. In order to account for this unusually unsaturated behavior, the plausible hypothesis was formulated that the two groups, $(\text{C}_6\text{H}_5)_3\text{C}$, failed to remain in permanent union with each other, that a spontaneous dissociation of the dimer into the monomer was taking place until an equilibrium was established:



In terms of the older chemistry, we had here free radicals of the order of the methyl; in terms of the modern structural chemistry, it meant that

the substance had one carbon atom which functioned not in the normally quadrivalent state, but only as trivalent.

It was quite natural that there should have been hesitation, and even reluctance, to accept the views advanced. While the strictly chemical evidence appeared reasonably convincing, the molecular weight of the surmised triphenylmethyl indicated, within experimental error, an ethane rather than a half molecule, at least at normal room temperature. It looked as if the history of cyanogen, cacodyl, ethyl, etc., would repeat itself on triphenylmethyl. But when it was found (Schlenk, Gomberg) that some other triarylmethyls—which in every other chemical respect were analogous to the triphenylmethyl—did possess a molecular weight corresponding to that of free radicals, then it was realized that triphenylmethyl has a real existence, that it is present in solution in the monomeric state only in slight amounts, and is in dynamic equilibrium with its dimer, and that the extent of such spontaneous dissociation must depend upon the nature of the six radicals in the ethane molecule. By 1910 it became universally recognized that the isolation of free radicals was an accomplished fact. At the present time there are known to exist almost two hundred substances, each indisputably with a carbon atom in the trivalent state. Trivalence of carbon is no longer considered anomalous; it is encountered infrequently because substances of this type are too reactive to persist under our everyday methods of experimentation, and they undergo rapid change into more stable systems.

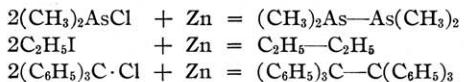
Anomalous Valence in Elements Other than Carbon

After it had been definitely established that our conception of valence constancy in carbon had been erroneous, it has proved possible to prepare also radicals wherein elements other than carbon function in anomalous states of valence. In nearly all cases the element under investigation was loaded to its limit with phenyl or other aromatic groups, since that kind of configuration had proved so successful in the case of the carbon atom. Radicals are at present known with nitrogen bivalent (Wieland, Goldschmidt) instead of the usual trivalent; with sulfur (Lecher) or oxygen (Pummerer, Goldschmidt) as univalent; tin (Rugheimer, Kraus) and lead (Kraus) as trivalent; with silicon (Kipping) presumably as trivalent; with boron as quadrivalent; with chromium as quadrivalent and univalent; and with arsenic as bivalent. For lack of time we shall limit ourselves on this occasion to the consideration of such radicals as contain trivalent carbon, and even these can be treated only briefly.

Radicals with Trivalent Carbon

Preparation.—(1) As regards methods of preparation, we still have to depend largely upon the same general method which was used by Bunsen

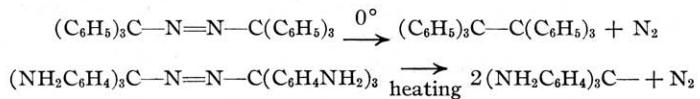
for the preparation of the supposedly free cacodyl, by Frankland for the ethyl, and which was also employed in the preparation of triphenylmethyl:



The solvent is benzene, ether, carbon disulfide, or some other non-reactive substance and all operations should be carried out in an atmosphere of carbon dioxide, hydrogen, or nitrogen. The metal may be Zn, Cu, Ag, Mg, Hg. Of these, molecular silver offers best advantages.

(2) Conant has employed successfully vanadous chloride. This method is likely to prove most useful in those cases where the carbinol halide is too unstable and is therefore inaccessible, while the carbinol itself is still sufficiently stable to be used. It is interesting that stannous chloride seems to be analogous to vanadous chloride in this respect. The carbinol is reduced to free radical.

(3) Thermal decomposition of complex substances has at times been employed for the preparation of free radicals. Thus, azo-triphenylmethyl decomposes at 0°, and a similar reaction has been used by Wieland, as a last resort, in the preparation of the para-rosaniline radical:



(4) Electrolysis of metallo-organic compounds, such as zinc ethyl, or of triarylmethyl halide, has been successfully employed for the preparation of free radicals.

The Proofs That Establish Existence and Degrees of Dissociation.—The diagnosis by strictly chemical means may be extremely suggestive but is not always fully convincing. When the dissociation of the hexa-arylethane in solution happens to be sufficiently large, then cryoscopic determinations of the molecular weight should tell the story of the dissociation fairly accurately. When, however, the degree of dissociation of the di-radical into the mono-radical happens to be so slight as to come within the range of usual error in cryoscopic measurements, *i. e.*, 3 to 8%, recourse can be had to colorimetric evidence. Experience in our laboratory has been that even those ethanes which show in solution complete dissociation are still colorless, or only slightly colored, in the solid state. Others have reported differently. Be that as it may, there is however complete agreement on these two points, namely: (1) there exists, even in solution, the colorless and the colored modification in equilibrium with each other; (2) there occurs an increase of color on further dilution of the hexa-arylethane solu-

tion. This behavior constitutes a deviation from Beer's law, and is explainable by the assumption that dilution increases the extent of dissociation of the colorless ethane into the colored radical, which is in harmony with the general effect of dilution on all forms of dissociation phenomena. Whether formation of a free radical is an all-sufficient explanation for the color production, or whether one must assume that there is an additional tautomeric change with a constant equilibrium—colorless mono-radical \rightleftharpoons colored mono-radical—need not be discussed here. Suffice it to say that the intensity of color in either case should be, and by recent calculations and experiments (Walden, Wooster, Ziegler) has been proved to be, proportional to the degree of dissociation. The colorimetric method therefore should be more reliable than the cryoscopic methods for measuring quantitatively the extent of dissociation of the hexa-arylethyanes.

There are many cases where dissociation is so slight that the solution of the ethane is colorless, and yet the ethane absorbs oxygen more or less readily, indicating at least a tendency toward a scission into two half-molecules. In such instances, heating the ethane in high-boiling solvents, xylene or anisol, will nearly always induce an increase of dissociation to such an extent that color will become visible. Then again there are cases when the ethane in solution develops no color even on heating, and does not absorb oxygen. It still is possible to get an indication of a potential dissociation through the effect of metallic potassium or sodium-potassium alloy. These reagents split such ethanes with the production of R_3CK compounds. Here, however, we enter upon debatable ground.

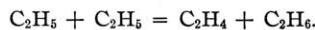
Some Properties of the Free Radical

Stability.—Triphenylmethyl itself, in the solid state, is quite stable. A sample, after twenty years of storage, was found to absorb just as much oxygen as when first prepared. Other triarylmethys differ very widely as regards stability; some decompose in a few hours, and others by the time their solution is concentrated to dryness.

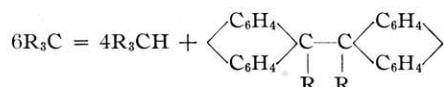
Color.—When dissolved, the radicals show each a characteristic selective absorption of light; solutions representing every color in the spectrum have been obtained. Triphenylmethyl is yellow-orange. Methyl groups in the side-chain of the benzene nucleus intensify the color toward orange; methoxy groups, more toward red; one *p*-nitro group induces deep green; three nitro groups, an intense fuchsine-like color. On exposure to air, the color is discharged and insoluble peroxides are formed.

Disproportionation.—It is a well-established fact that, occasionally, in a Grignard reaction when ethyl magnesium bromide is used, the ethyl radical does not attach itself to the carbon atom, but is set free. For some reason, however, it fails to be completely converted into the dimeric form, butane. Then we have the occurrence of disproportionation. One ethyl

robs the other of a hydrogen and there result equal amounts of ethane and ethylene:



A similar disproportionation may be induced in triphenylmethyl by photochemical or thermal effects, one part becomes hydrogenated to triphenylmethane, while another portion loses hydrogen from the nucleus:

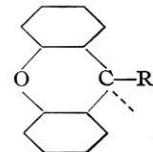
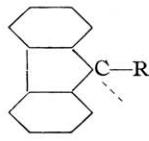


Molecular Combinations.—One of the most striking characteristics of the parent-substance, triphenylmethyl, is that it forms molecular combinations with practically every solvent in which it may be dissolved—aliphatic, alicyclic, and aromatic hydrocarbons, ethers, esters, aldehydes, nitriles, carbon disulfide, chloroform, etc. On gentle warming, the solvent of combination or crystallization, can be removed. It may appear strange that other triarylmethyls, which are far more persistently monomolecular than triphenylmethyl, seem to be devoid of this extraordinary combining capacity. It is, however, possible to find a plausible explanation, but we shall not enter into it here (Gomberg, *Chem. Reviews*, 1, 109).

Irreversible Combinations and Chemical Reactions.—The triarylmethyls, as a class, are among the most reactive substances known. In addition to their characteristic reaction of forming peroxides with oxygen, and with halogens regenerating triarylmethyl halide, there are a large number of other, more or less irreversible, spontaneously occurring reactions. The radicals combine with hydrogen, sulfur, nitric oxide, nitrogen tetroxide, sodium, (MgBr), quinone, diazomethane, etc.; they react with phenol, xylene, phenyl hydrazine, to mention but a few.

Varieties of Trivalent Carbon Radicals

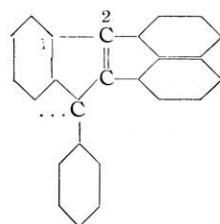
The earliest type of triarylmethyl radicals consisted mostly of members wherein the three phenyl groups varied in containing side groups; *i. e.*, tolyl, methoxy-phenyl, halogenated phenyls, naphthyl, biphenyl, etc., replacing one, two, or all three phenyl groups in the original triphenylmethyl. As an extension of that group may be considered also such triarylmethyls in which two of the aryl groups are either directly or indirectly in combination with each other forming a biphenylene, xanthane, thioxanthane, or acridine ring.





Each of these four classes presents its own specific characteristic properties, but by far and large these radicals differ only in degree and not in principle from triphenylmethyl itself. In general, it may be said that the biphenylene type tends far more toward dimerization of the radical, while interposition between the two aryl groups of an oxygen atom, a sulfur or a nitrogen atom, often induces complete dissociation of the ethanes into free radicals even at room temperature.

In a class somewhat by themselves are those radicals wherein at least one of three groups is not an aromatic group at all. Kohler, as far back as 1908, determined the existence of such a case in the indyl compound. In this, the trivalent carbon atom is linked directly to two aryl groups only,

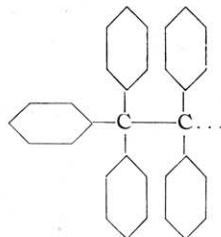


the third valence being linked to an unsaturated ethylene group. A large number of variations of this general type of free radicals has become known through recent work by Ziegler, by Lowenbein, Conant, Marvel, and others. These variations consist largely in interposing an oxygen atom between the two carbon atoms marked in the above formula as 1 and 2.

That such a change is likely to enhance the stability of the monomeric radical is to be inferred from the effect of the influence of the oxygen atom in the xanthene series. The noteworthy fact in all these instances is that an aliphatic group which contains an ethylene or an acetylene linking may become more or less equivalent to an aryl group as regards imparting stability to radicals, *i. e.*, propensity of diradical to dissociate.

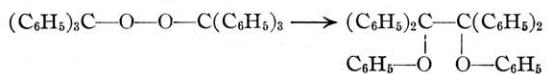
Largely through the efforts of Conant and co-workers, a considerable number of hexa-substituted ethane compounds have been prepared in which one of the three groups on each of the ethane carbon atoms is a saturated aliphatic group—methyl, benzyl, ethyl, propyl, *n*- and iso- and tertiary butyl, amyl, etc. In this class also, if the two aromatic groups are joined by an oxygen atom and form a xanthone ring, then a much greater tendency is shown by the ethane to dissociate into free radicals.

Pentaphenylethyl (Schlenk) is an example of a free radical which contains one aliphatic and two aromatic groups.

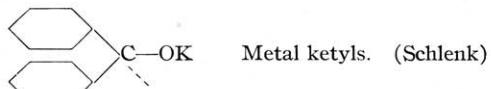


I am not aware that any successful attempts have been made in preparing free radicals which contain only one aromatic and two aliphatic hydrocarbon groups linked to the central carbon atoms. Recent work, particularly that by Marvel and his co-workers, suggests that some ethanes which contain four and six acetylene linkings approach in their dissociation behavior hexa-arylethyne.

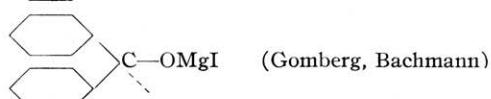
A few words concerning still a different class of dissociable ethanes. Wieland, twenty years ago, showed that the peroxide of triphenylmethyl on heating to 140° undergoes an intramolecular rearrangement:



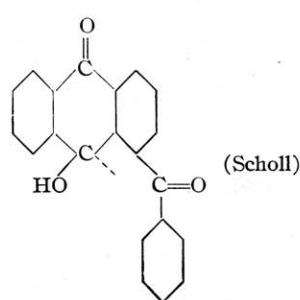
The resulting ethane shows a slight tendency to dissociate, when heated, into free radicals. Since that time several classes of similarly composed radicals have been prepared, namely, those wherein the central carbon atom is attached to two aryl groups and by the third valence is attached to an oxygen atom.



Metal ketyl. (Schlenk)



(Gomberg, Bachmann)



(Scholl)

This talk would not be complete without at least bare mention of the striking investigations by Paneth, who demonstrated the transitory existence of the radicals, methyl and ethyl, with a half-life period for the former of 0.006 of a second. Paneth's results go far in making it appear more certain that in many chemical reactions free radicals, with momentary but decidedly measurable periods of existence, are intermediate products. May I refer to the very happy application of this idea by H. S. Taylor and by F. O. Rice, in their recent interpretation of the thermal decomposition of aliphatic hydrocarbons?

Thus, between these two extremes in the chronological sense, the triphenylmethyl of 1900 and the methyl of 1929, we have become definitely aware that liberation and formation of free radicals is a general occurrence in chemical reactions; that some are stable enough to withstand mutual collisions and so continue to retain their entities; others after a brief period of independent existence, unite with each other, or react, on collision, with molecules of other substances.

Conclusion

For the purposes of this review, it appeared somehow more desirable to adhere rather closely to matters of reasonably well-established facts, in preference to taking up the discussion of controversial phases of the subject. The reviewer is aware of the incompleteness of such a treatment. Many questions obtrude themselves: What factors actually determine the tendency of dissociation in a substituted ethane? Is it weight and volume of the substituting aryl groups, or is it their peculiar chemical constitution? Why do two such substances as the biphenylene and the xanthone hexa-arylethanes, both of almost identical molecular weight, differ in dissociation degree from practically zero in the one to 100% in the other? How explain the fact that naphthyl, when replacing phenyl, enhances the persistence of the monomolecular state of the radical very markedly, and yet when it is a component in the xanthone ring, its influence is of the opposite character? If the electrochemical nature rather than the size of the aryl group is the determining factor of the dissociation capacity on the part of the ethanes, how explain that the strongly electropositive trimethoxy-triphenylmethyl and the strongly electronegative trinitro-triphenylmethyl are both equally persistent in the mono-radical state? If the heat of dissociation of hexaphenylethane is only 11.5 kg. cal. (Ziegler), as compared with 70 kg. cal. for the normal value for bond of carbon to carbon, may not this be due to the fact that the three phenyl groups on each of the two carbon atoms hinder stereally the latter from approaching each other to within 1.5 A. U., as carbon atoms normally do in diamond? Another question—is there a difference in chemical structure as well as in the character of the electric charge in the three isomers, the neutral radical

triarylmethyl, the triarylmethyl anion in $(C_6H_5)_3C^-Na^+$ and the cation in $(C_6H_5)_3C^+Cl^-$? Is it probable, as has been assumed (Zelinski, Staudinger) to be the case, that two carbon atoms within the same molecule but not contiguous, may each function as trivalent? And what—if one may dare to put the question—of two contiguous carbon atoms, as for instance in tetranaphthyl-ethylene? Some day we shall have definite answers to all these questions.