ON THE CHEMICAL MECHANISM OF ORGANIC REARRANGE-MENTS.

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In a later paper on "Ring Formation and the Strain Theory," the analogy between the course of rearrangements in cyclic and acyclic derivatives will be discussed from the affinity-energy-spatial relations of the atoms, and, as a wide discrepancy is found in chemical theory in regard to the cause and the mechanism of such changes, it seemed desirable for a correct understanding of the correlation to consider beforehand the subject of rearrangement from the same point of view.

In a homogeneous chemical system, an intramolecular rearrangement takes place through a change in the positions of certain atoms or groups of atoms in the molecule, and the new, isomeric product may belong to the same, or to a different chemical type; in the latter case the process may be called a *type rearrangement*. When the isomerization takes place intermolecularly, it proceeds with the dissociation of the substance into simpler parts, which then unite to form a compound that is more stable under the conditions of the experiment.

In a heterogeneous chemical system, the change in the chemical structure may occur with the loss of a component part of the substance, through the catalytic influence or the chemical action of the energy in the reagent, with isomerization of the residual structure. Or, by the union of the substance with the reagent, when, owing to the chemical energy thus added, an isomerization in the substance part of the "polymolecule" takes place with partial conversion of its free energy into bound energy and heat, and is followed by the breaking down of the system into the isomerized substance and the reagent. Reactions of this class are always type rearrangements.

The factors that determine an intramolecular rearrangement are: first, the extent of the free chemical energy at the interchanging atoms or groups of atoms; second, their affinity for each other and for the atoms in the group to which they migrate; third, the amount of energy required to separate the migrating parts from the remaining atoms of the group, which constitutes a hindrance to the arrangement, and, finally, the heats of formation of the isomerides or the two products. As these factors may now be connected with the chemical structures of organic substances, an analysis of the changes from this standpoint is an explanation of the rearrangement.

The conversion of iso- into tert.-butyl bromide is an excellent illustration of direct isomerization, and of the subtle relations that may determine stability towards heat energy. In the methinyl group of the iso-

derivative the affinity between the carbon and hydrogen has been greatly decreased by the numerous, adjacent hydrogen atoms,[1] and, as the tert. bromide has a greater heat of formation, the affinity and energy relations exist in the primary bromide for a facile, direct isomerization. What is considered an unusually pure preparation of isobutyl bromide is stable considerably above its boiling point, but this stability is due to the presence of an anticatalyte in infinitesmal quantity, as the purest product obtainable changes slowly into the tertiary compound at room temperature and rapidly far below the point of ebullition.[2]

The historic conversion of ammonium isocyanate into urea is an admirable example of isomerization through dissociation. All ammonium salts are broken down by heat energy more or less readily into ammonia and acid, and, whether the isocyanic acid (HOCN) thus set free keeps its structure under these conditions or is converted into the less acidic, intramolecularly better neutralized carbonimide (OCNH), is immaterial to the final phase of the reaction, as each of the forms is capable of adding ammonia; in the latter case forming directly carbonamide, and, in the former, an enol isomer which will pass over into that product.[3]

Although the chemical system is heterogeneous at the start, it is not infrequent that the actual rearrangement takes place in a homogeneous system. This may occur through the increment of chemical energy to the rearranging molecule by the formation of a "polymolecule" (catalytic rearrangement), by that of a real addition product of the substance and the reagent, or by the replacement of one or more of the atoms in the substance by other atoms or groups of atoms, whose affinity and energy relations favor the change. Thus, phenylhydroxylamine is a weak base, and, although the energy required to separate the hydroxyl group and a hydrogen of the aromatic nucleus from the respective groups is not very considerable, the free energy in the hydroxyl group is not large nor can there be a decided difference between the heats of formation of the substance and the isomeric aminophenol. Increasing the free energy, and decreasing the hindrance to an isomerization by the increment of heat energy, results in the intermolecular breakdown into aniline, azo- and azoxy-benzene and water. With the formation of acid phenylhydroxylamine sulfate, however, all the energy and affinity factors change favorably toward an intramolecular rearrangement. The weak base is now strongly overneutralized, and the product with its large surplusage of negative chemical energy not only works towards converting the weak basic component of the salt into a stronger base, whereby more of the excess of its free negative energy will be converted into bound energy and

[1] Michael, THIS JOURNAL, 32, 997 (1910).

[2] Michael and collaborators Ann., 379, 263 (1910); 393, 81 (1912); THIS JOURNAL, 38, 653 (1916).

[3] Michael, J. prakt. Chem., [2] 60, 411 (1899).

heat, but the affinity of the negative hydroxyl group for a hydrogen of the aromatic nucleus has been increased, and the energy necessary to separate them out of the groups in which they are placed has been greatly decreased. *With the formation of acid aminophenol sulfate[1] a considerable entropy increase must, therefore, take place; indeed, it is an invariable rule in the intramolecular rearrangements of all acidic and metallic organic derivatives, that the changes occurring in the structure of the mother substances are of a nature to neutralize the surplus of free energy existing in the salts.[2] And, it is an unfailing characteristic in all such molecular reconstructions that they proceed with an increase in the entropy of the system; that is, by a greater conversion of the free into bound energy and heat than the opposite energetic changes.*

One of the primary conditions for intramolecular rearrangement without dissociation is the accumulation of free energy in considerable amount at one of the atoms or group of atoms in the molecule. Thus, while phenylhydroxylamine decomposes readily at 100° into various products and water, phenylchloroamine or phenylnitramine, in which the weakly negative hydroxyl group is replaced by the strongly negative chlorine atom, or nitro group, with the aid of the greater amount of unneutralized, free chemical negative energy in them, are readily transformed into the intramolecularly much better neutralized, chloro- and nitro-aniline.

The Amide ⟶ Amine Rearrangement.

Hofmann[3] showed that the bromoamides are converted into isocyanates on treatment with silver carbonate, and Tiemann[4] first suggested that the latter are intermediate products in the Hofmann amine synthesis, a view which was proven experimentally by Mauguin.[5] Tiemann[6] also indicated

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[1] The further analysis of this rearrangement will appear in a paper on the structure and properties of benzene and its derivatives.

[2] The most casual examination of this subject in chemical literature and in textbooks, will suffice to show that these conditions cannot be too strongly emphasized. It will be noticed, that rearrangements are frequently assumed to take place with substances that are in themselves either perfectly stable, or, when heated sufficiently, decompose in an entirely different manner. It is certainly remarkable that so many typical rearrangements should still be theoretically misinterpreted in this way, as, for instance, with the transformation, at a high temperature, of methylaniline-iodo- and chlorohydrate into the corresponding salts of *o*-, and *p*-toluidine, respectively. In this case, the so self-evident explanation has been known for many years (Michael, *Ber.*, 14, 2107 (1881)) *i. e.*, that the isomerization must take place through the dissociation of the salts into aniline and the methyl halide. They can now only react differently on each other, as they cannot reunite under the prevailing conditions of temperature, the halogen atoms attacking the easily replaceable hydrogen in the aromatic nucleus of the base, with the formation of salts of the more strongly basic toluidines.
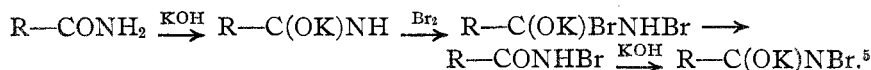
[3] *Ber.*, 15, 412 (1882).

[4] *Ibid.*, 24, 4163 (1891).

[5] *Compt. rend.*, 149, 790 (1909); *Ann. chim.*, [8] 22, 310 (1911).

[6] *Ber.*, 15, 4164 (1891).

that the antecedent step in this reaction, and the formation of aniline through the isocyanate in the distillation of benzohydroxamic acid, consisted in the formation of the unstable structures $RC(O)N$. This now very generally accepted interpretation was developed and extended to other similar reactions by Stieglitz,[1] who ascribed the rearrangement to "the free or latent valences at the nitrogen atom," and later,[2] in agreement with Jones,[3] to a shifting of electrons from carbon to nitrogen.

Hantzsch[4] has given experimental evidence in favor of enol structures for the potassium acyl bromo-amides, which are probably formed as follows:

$$R\text{---}CONH_2 \xrightarrow{KOH} R\text{---}C(OK)NH \xrightarrow{Br_2} R\text{---}C(OK)BrNHBr \longrightarrow$$
$$R\text{---}CONHBr \xrightarrow{KOH} R\text{---}C(OK)NBr.[5]$$

[1] Am. Chem. J., 18, 751 (1896); 29, 49 (1903). The literature on the subject, and a dicussion of other interpretations of the rearrangement, may be found in these papers.

[2] THIS JOURNAL, 36, 288 (1914); 38, 2047 (1916).

[3] Am. Chem. J., 50, 441 (1913).

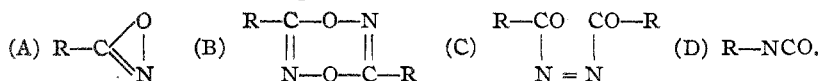[4] Ber., 35, 252 (1902). See also Stieglitz, Am. Chem. J., 29, 49 (1903).

[5] Schroeter (Ber., 42, 2337, footnote 4 (1909)) believes that the formula $R\text{---}CONKBr$ is equally well established, since it is impossible to decide which of the desmotropic forms, $R\text{---}C(OH)NBr$ and $R\text{---}CONHBr$, is the more acidic, and the hydrogen of "ammonia residues" may have "strongly acidic character," e. g., in hydrazoic acid. The latter statement appears somewhat exaggerated, as the affinity constant of the acid at $0°$ is only 1.10^{-5} (Hantzsch, Ber., 32, 3066 (1899)). Although the fundamental principles governing the structural rearrangements that may take place with the conversion of neutral organic substances into metallic derivatives were fully developed in 1887 (Michael, J. prakt. Chem., [2] 37, 473 (1888); Am. Chem. J., 10, 158 (1888); 14, 481 (1892)), there seems to be still some uncertainty on the relation of such changes to the chemical composition and the structure of the substances.

An accumulation of negative energy must result when a number of nitrogen atoms are grouped together, as in hydrazoic acid, but the strength of its acidic manifestation depends also on a second factor, viz., that the negative energy at the nitrogen group is largely in a free state. It is this condition of the negative energy that gives that acid its chemical resiliency towards positive chemical energy; if the free energy at the 3 nitrogen atoms had been converted into bound energy in forming the group, to the extent that takes place in forming the nitrogen molecule (THIS JOURNAL, 32, 990 (1910)), it might act almost neutral towards water, or even towards weak bases.

The quantity of negative energy in the oxygen of benzoamide is not only greater than that of the nitrogen, but also its quality towards that in the potassium atom, and a relatively larger proportion of it is in a free, chemically more potential, condition. The action of potassium on benzoamide can take place, therefore, only at the oxygen atom; in driving out a hydrogen and forming at once $C_6H_5\text{---}C(ONa)NH$, the maximum entropy of the system is attained, and no further structural change can occur under the experimental conditions (ibid., 1002).

Even Hantzsch (Ber., 35, 229 (1902)), who has contributed experimentally so much to confirm the writer's views, has not fully understood the subject, for he believes that in an organic product sodium always joins on to oxygen in preference to nitrogen, and, for that reason, sodium cyanoacetic ester has the structure $NC\text{---}CH = C(ONa)OE$. The nitrogen in a nitrile group is always rich in free energy, and the quality

The affinity-energy-spatial relations of the metal and halogen in these derivatives are extremely favorable for interaction, for the mother-substances are not very acidic[1] and, therefore, in each of these atoms there must be still considerable free chemical energy of an opposite character; besides, the affinity of bromine for nitrogen is only slight, and the metallic and halogen atoms are in the spatially closest possible positions (1,5). With the elimination of potassium bromide a structural change must take place, for there is an enormous amount of free negative energy at the nitrogen and oxygen atoms of the residual structure CH_3—C(O)N, and, as they are both in direct union with carbon, they have greatly reduced the affinity between the carbon atoms. A chemical reconstruction in 6 directions[2] is now possible

$$\text{(A) } R-C\underset{N}{\overset{O}{\big<}} \quad \text{(B) } \begin{array}{c} R-C-O-N \\ \| \quad\quad \| \\ N-O-C-R \end{array} \quad \text{(C) } \begin{array}{c} R-CO \quad CO-R \\ | \quad\quad | \\ N=N \end{array} \quad \text{(D) } R-NCO.$$

The second law of thermodynamics demands that in the spontaneous chemical change that follows the primary phase, the free energy in the unstable structure shall pass over to the maximum possible extent into bound energy and heat; the chemical limitations to the realization of this goal are, the affinity relations between the atoms, and the energetic hindrances to a transformation. The formation of (A)[3] involves the considerable in cyanoacetic ester for sodium has been increased through the negative influence of the oxygen atoms. On the other hand, when the hydrogen of a carboxyl group is replaced by alkyl, the negative energy of the oxygens is neutralized to a more or less considerable extent, and it is primarily the free energy that is converted. The magnitude of this loss of negative energy in the esterification of the carboxyl group is shown by the incapacity of benzylacetic ester to form a *merotropic* sodium derivative, and the greater *chemical potential* (*Ann.*, 363, 21 (1908)) in the CN than in the COOE group for sodium, that such a product may be obtained from benzylonitrile. That a greater neutralization of negative energy occurs by the union of the metal to the nitrogen of cyanoacetic ester is also evident from the fact that the compound is decidedly more acidic than malonic ester (see *Am. Chem. J.*, 43, 358 (1910)).

It would certainly add to clearness in chemical terminology in this field, and to precision in the theoretical conceptions, if the suggestion (Michael, *Ann.*, 363, 20 (1908)) were adopted, that the terms tautomerism, or desmotropy, be used only to designate the capability of certain substances to exist in, and to pass over intramolecularly into, forms with different chemical structures, and *merotropy* to that of substances passing over into a derivative of a desmotropic form, through the combined influence of the affinity-energy relations in a heterogenous chemical system. The phenomena are closely related, but not necessarily coincident (*ibid.*, 31–35).

[1] Hantzsch, *loc. cit.*, states that the salt reacts alkaline towards litmus, but may be titrated with alkali by using phenolphthalein.

[2] The very improbable intermediate formation of $\overline{CH_2 - O - NH}$ is not taken into consideration. See Hesse, *Am. Chem. J.*, 29, 56 (1903). The affinity-energy conditions exist for the formation of R — O — CN, but the entropy increase in that case would be much less than with that of R — NCO.

[3] Hantzsch, *Ber.*, 27, 1256 (1894); Stieglitz, *Am. Chem. J.*, 29, 65 (1903).

expenditure of energy to shift the segmentations of the oxygen and nitrogen spheres on the carbon sphere,[1] to the large extent necessary for forming the 3-membered ring derivative, which can be effected only by the free energy at the nitrogen and oxygen atoms. The change in this direction is debarred, however, for the affinity between these elements is too slight for them to perform so large a work. It is remarkable, therefore, that such a cyclic arrangement not only exists in *phenyl-cyclo-nitrile oxide*,[2] but it is formed in a closely allied reaction, *viz.*, in the spontaneous decomposition of sodium benzohydroxamic chloride, $C_6H_5C(NONa)Cl$.[3] The energy-spatial relations of the metal and halogen in that product are strictly comparable to those of the similar elements in the potassium acylbromoamides, and the outward analogy between the two decompositions is so striking that Wieland[4] investigated the problem whether such cyclic nitrile oxides are not the primary intermediate products in the Hofmann amine reaction. Although the phenyl derivative is partially converted by heat energy into the isocyanate, the interpretation had to be given up, as the substance could not be prepared from benzobromoamide, nor is aniline formed in its decompositions.

Why do two structurally and energetically so similar classes of compounds as $RC(NONa)Cl$ and $RC(OK)NBr$ give so entirely different products of decomposition? With the replacement of the hydroxyl-hydrogens in a hydroxamic chloride and enol bromoamide by a metal, a considerable transformation of its free energy and that in the halogens into bound energy takes place through space, which must result in these atoms being brought closer together spatially. This change evidently carries with it an approachment of the elements joined directly to the metal and halogen, that is, their segmentations on the respective carbon atoms are brought nearer together; a spatial juxtaposition that increases when the halogen and metal enter into direct union, and pass out of the

[1] Michael, THIS JOURNAL, 40, 705 (1918).

[2] The usual names, phenylnitrile oxide, and also benzonitrile-N-oxide (Richter's "Lexikon," 1910–11, 344), are chemically ambiguous. Besides cyclo, the prefix *epi* may be used to designate ring formation, as it is already connected in chemical nomenclature with such a structural condition; for instance, epichlorohydrol. Votoček (*Ber.*, 44, 360 (1911)) has suggested prefixing *epi* to distinguish diastereomeric derivatives, and to designate the appearance of such products as *epimerism*. Although this suggestion was adopted in Meyer-Jacobson's "Lehrbuch" (I³, 912), it cannot be considered an apt addition to chemical terminology, since *epi*, as stated above, is already connected with an entirely different chemical relationship, and there is absolutely no connection between the derivation of the prefix and its use to characterize *diastereomerism*. The latter term is far superior to *epimerism*, and, instead of *epi*, it would be better to prefix *diastereo-;* or *diaallo-*, e. g., glucose and diastereo- or diaallo-glucose.

[3] Werner, *Ber.*, 27, 2199 (1894); Wieland, *ibid.*, 40, 418, 1667 (1907); 42, 803 (1908).

[4] *Ibid.*, 42, 4207 (1909); see also Schroeter, *ibid.*, 42, 2339 (1909).

system as a salt. The quantity of the free energy at the Δ-C and Δ-O, respectively the Δ-N and Δ-O, obviously now becomes very considerable, but the capability of these atoms to overcome the hindrance to form a 3-membered ring, evidently depends also on the quality. The affinity of carbon for oxygen is highly developed, while that of nitrogen for oxygen is correspondingly slight, and, in this contrast in the affinity values of the end Δ-atoms of the intermediate structures, is to be found the striking difference in the following phases of the reactions.[1]

Formula B represents a more stable structure, in whose formation an entropy increment over that by (A) would ensue, as the energetic hindrance to the development of its 6-membered ring is smaller than that in the tricyclic arrangement in (A). The chemical obstacle is, however, the slight affinity between the nitrogen and oxygen atoms. It is again an affinity relationship that prevents the realization of (C), as the direct union of the negative acyl radical with the nitrogen has so materially diminished the attraction between nitrogen and nitrogen that such a structure could show but a very slight stability towards heat energy. Moreover, the free energy content of (C) would be quite large; considerably greater than that of (B), and probably only slightly less than that of (A). All the energetic relations in the unstable complex favor rearrangement according to the Tiemann-Stieglitz interpretation, which finds its expression in (D). In the first place, the hindrance to the migration of the *hydrocarbyl*[2] group is slight, as the affinity between the carbon atoms has been greatly decreased by the direct negative influences of both the oxygen and the nitrogen atom, while, on the other hand, that of the nitrogen for the hydrocarbon group, is decreased comparatively much less, as the influence of the oxygen is only indirect. That the affinity between *hydrocarbyl* and nitrogen in isocyanates is decidedly developed is evident from the properties of the substances, for in none of their chemical decompositions does the rupture occur at that point. Finally, in regard to conversion of the

[1] When an organic compound contains atoms that may interact on each other, an intramolecular decomposition is favored if these atoms are spatially near to each other, or, if the atoms joined directly to them are in the same steric relationship (Michael, *J. prakt. Chem.*, [2] 60, 335 (1899)). In the first case, the question of a monomolecular ring formation depends more on the affinity relations of the atoms that become momentarily unsaturated than in the second, as they are farther apart spatially, and the energetic hindrance is therefore greater. Sodium chloroacetate does not give a tricyclic derivative, because the carbonyl group reduces the affinity between the methylene carbon and the natroxyl oxygen so much that they are not able to overcome the energetic hindrance, but replacing the carbonyl by the methylene group, *i. e.*, sodium ethylene chlorohydrol, increases these affinity relations sufficiently to lead intramolecularly to the cyclic ethylene oxide.

[2] This word is suggested as a generic name for any *monovalent* hydrocarbon radical, irrespective whether it is saturated or unsaturated. *Hydrocarbene* and *hydrocarbine* might be used to express collectively ethylenic and acetylenic hydrocarbon derivatives.

free energy in the unstable system, there can be no doubt that it is greater in the formation of (D) than it would be in that of (A) and (C), and probably there is only a small difference between it and that of (B).

Rearrangements in Aliphatic α,β-Glycols.

In no other class of organic rearrangements are the chemical changes more complicated and dependent on chemical structure than those accompanying the loss of water in the α,β-glycols. The theoretical interpretation of this subject is difficult or impossible from the current theoretical views, and it offers an excellent test of the applicability of the affinity-energy-spatial view-point to a very intricate problem in organic theory.

Under ordinary conditions, glycol must have a fumaroid configuration,[1] which is the spatial form favoring the intramolecular elimination of water,[2] when only one of the hydroxyl groups is involved in the process. Simultaneously with such a dehydration, either a gyration of the methylene radical on the common carbon axis, or a migration of the hydrogen of the hydroxyl to the place occupied before by the abstracted hydroxyl, must take place.[3]
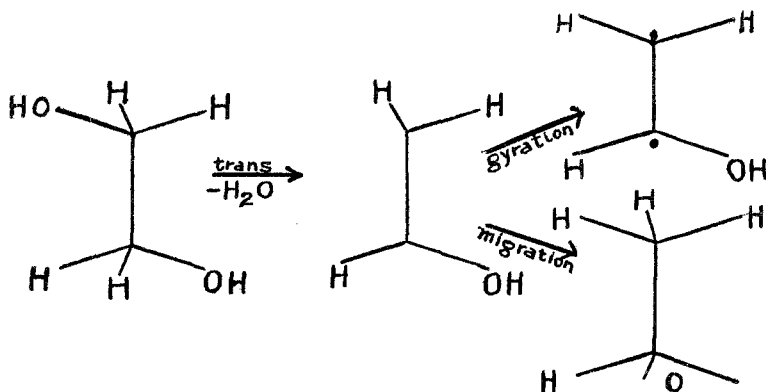
Fig. 1.

These changes require each the expenditure of a certain amount of the free energy in the unstable, intermediate configuration, and that of the

[1] Michael, THIS JOURNAL, 40, 707 (1918). The reasons there stated for the fumaroid stereostructures of monobasic acids apply to all saturated organic substances.

[2] Michael, J. prakt. Chem., [2] 52, 359 (1895).

[3] The absence of an atomic symbol always implies a carbon atom. Unsaturation is shown by one or two points over or below the atoms (Michael, J. prakt. Chem., [2] 46, 204, 222–254 (1892)), and the shorter lines between unsaturated than between saturated atoms denotes that the centers of the atoms in the unsaturated group are nearer together than those in the corresponding saturated group (Michael, THIS JOURNAL, 40, 706 (1918)).

two possible products will be formed in which it is more completely transformed into bound energy and heat, *i. e.*, in which the maximum entropy of the transformation is realized. This result is attained in aldehyde (2),[1] as vinyl carbinol (1) evidently represents an intramolecularly much less neutralized system.[2]

The second possibility (B) in the intramolecular elimination of water from glycol, involves the two hydroxyl groups, which, judging from anal-

[1] The spatial interpretation given above differs somewhat from Erlenmeyer's (*Ber.*, 13, 309 (1880)) explanation, which assumes that aldehyde is formed only through the intermediation of vinyl alcohol. See also Tiffeneau, *Compt. rend.*, 137, 12-60 (1903); Tiffeneau and Dorlencourt, *ibid.*, 143, 126 (1906).

[2] According to Krassusky, Type A does not correctly represent the conversion of glycols into aldehydes or ketones. The interesting researches of this chemist on this subject were published in full only in Russian, and the most complete account of them available to the writer was found in Liebig's *Jahresber.*, 55, 783 (1902). Krassusky showed that the α-alkylene oxides are isomerized by $ZnCl_2$ into aldehydes or ketones at a much lower temperature than that of the conversion of the corresponding α,β-glycols, and that glycols are obtained by heating the α,β-chlorohydrols with water in sealed tubes, while oxides are formed in the presence of PbO (*ibid.*, 988). Further, that the chlorohydrols distilled with PbO or Ag_2O give oxides, while aldehydes or ketones are obtained with ZnO, and Krassusky concluded, therefore, that the formation of the latter products always proceed through that of an oxide. As the α,β-glycols are converted by heating with conc. HCl into the chlorohydrols, Krassusky believed that the transformations of an α,β-glycol into an aldehyde or ketone primarily goes through that stage, then into the oxide, and that the latter substances, besides the normal addition products, *i. e.*, chlorohyrols, may give the hypochlorous esters in small amounts which would decompose into HCl and an aldehyde or a ketone. The reformed chlorohydrols would again yield oxides, and the cycle of above processes would go on until the glycol is all converted into aldehyde, ketone, or mixture of them. (See, also, Krassusky, *J. prakt. Chem.*, [2] 64, 392 (1901), and Nef, *Ann.*, 335, 243 (1904)). The various stages of this explanation are possible only on paper. The glycols are transformed into aldehydes and ketones under conditions of dilution of acid that the reverse reactions rather than the formation of chlorohydrols would take place. Further, the oxides only add hydrochloric acid in concentrated solution to form the chlorohydrols, and the simultaneous formation of hypochlorites is inconceivable from the energy standpoint, as they would represent a spontaneous degradation in the entropy of the systems; moreover, this reaction has been very carefully examined without the least indication of their appearance (Michael, *Ber.*, 39, 2785, 2789 (1906)).

The isomerization of the oxides by $ZnCl_2$ may proceed catalytically through the formation of a "polymolecule," or by that of an addition product with the energetic reagent:

$$CH_2 - CH_2 + ZnCl_2 \longrightarrow CH_2(OZnCl) - CH_2Cl \longrightarrow CH(OZnCl) =$$
$$\underset{\llcorner O \lrcorner}{} \qquad\qquad\qquad CH_2 + HCl \longrightarrow CH(OH) = CH_2 + ZnCl_2.$$

The oxides are transformed more readily than the glycols, because of their much larger free energy content; and because compounds of the ether type lose but little of it in forming double compounds with zinc chloride, whereas the union in the members of the alcohol type is accompanied by a large loss of energy as heat. That Type A isomerizations cannot take place from the chlorohydrols and water in the presence of PbO is evident, as it depends on the catalytic influence of free acid. Finally, in the distillation of the chlorohydrol with zinc oxide, besides ethylene oxide, $ZnCl_2$ is formed,

ogy to the stereomeric, dibasic acids, should take place through the maleinoid configuration:[1]
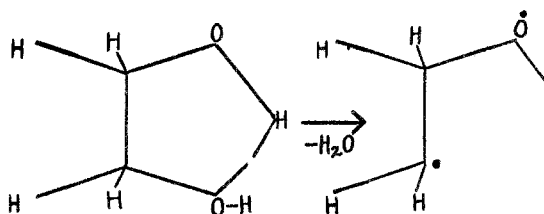
Fig. 2.

In this case, too, an unstable structure is formed, which may pass over, through migration of a hydrogen atom, into aldehyde; polymerize, through the union of two systems, to diethylene oxide, or directly form ethylene oxide.

The glycols, in which one to three of the nuclear hydrogen atoms are replaced by hydrocarbyl radicals, may lose water according to (A) and (B), but Type A is structurally prevented with the total replacement of these hydrogens. In the presence of an alkyl group, (R), a third type of elimination (C) becomes possible, and the intermediate structure thus formed may rearrange, by trans-migrations[2] of R and the hydroxyl-hydrogen, into a ketone:
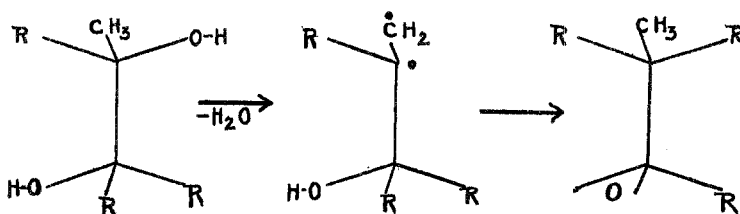
Fig. 3.

which is able to isomerize the oxide, whereas $PbCl_2$ and AgCl are without action upon it.

Markownikoff (Liebig's *Jahresber.*, **55**, 785 (1902); *J. Chem. Soc.*, **84**, 200 (1903)) appears to have suggested views somewhat similar to those of Krassusky, but as his paper, too, appeared only in Russian, it is impossible to form an intelligent opinion on them, and on the "principle of chemical equilibrium," from the résumés in non-Russian journals.

[1] This projection of the sphere configuration of glycol, and those of other substances in the paper, were obtained by connecting the centers of atomic spheres in direct union by straight lines, and extending the lines, when the spatial juxtapositions of certain atoms are to be accentuated, to the points on the surfaces that are nearest together in space. The actual spatial relations of the atoms are more accurately and clearly represented in this way than in the skeleton configurations now in use.

[2] The facility of the pinacol rearrangement indicates that the hindrance to trans-migration is slight; perhaps, like in the trans-addition and trans-elimination of the halogens and the halhydric acids (THIS JOURNAL, **40**, 1690 (1918)), less than that

The rearrangements with the fatty α,β-glycols take place with the use of more or less *dilute* solutions of strong acids, which cannot possess that direct, considerable affinity for water essential for the procedure according to (B). Whether the decomposition of the mono-, di-, and tri-substituted glycols proceed according to (C) or to that of (A) depends on whether more energy is required to remove the separate hydrogen atom used in the formation of the water from an alkyl radical than from the axial carbon in the carbinol group. As the influence of the hydroxyl diminishes the affinity between carbon and hydrogen more than that of an alkyl group, Type A represents the process in all but the fully substituted α,β-glycols. This relation has been demonstrated experimentally by the course of the rearrangements in the sec.-tert.-glycols; for instance, the decomposition of methyl diethyl glycol might take place according to Type C, and yield methyl diethyl aldehyde, but it actually takes place according to (A), and gives methyl isopropyl ketone.[1] And, it is also proven by the behavior of unsym. dimethyl glycol, on heating with the dehydrating mixture of acetic anhydride and sodium acetate, when the in-

occurring in the corresponding cis-process. There appears to be no doubt that ring-formation takes place through the cis-configuration, but the question may be raised whether, when it occurs with the loss of a component part of the substance, it is a direct process between the cis-groups, or a trans-elimination with a practically simultaneous rearrangement?

Thus, instead of succinic anhydride being formed from cis-succinic acid through the following stages

$$\begin{array}{ccc}
H_2C-COOH & H_2C-C(OH)_2 & H_2C-CO \\
| & | \quad \diagdown O & | \quad \diagdown O \\
H_2C-COOH & H_2C-CO & H_2C-CO
\end{array}$$

$\xrightarrow{} \qquad \xrightarrow{-H_2O}$
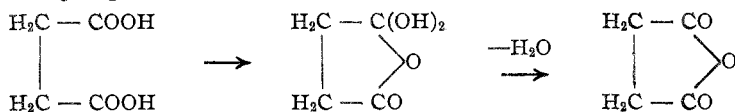
its formation may be expressed, stereostructurally, by
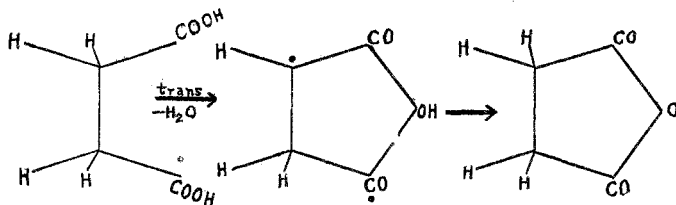
Fig. 4.

In this interpretation the long-standing conflict between the stereochemical conception of ring-formation, and the experimentally established addition-elimination relations, is avoided (*ibid.*, 1706). It may be mentioned that a third interpretation is possible, *viz.*, the dehydration proceeds through the formation of succinic mono-ketene, $HOOC-CH_2-CH=CO$. Anhydrides are easily formed intermolecularly from ketenes and acids, and, with the very favorable energy-spatial relations of the interacting groups in the ketene-acid, a spontaneous transformation into succinic anhydride would undoubtedly follow its formation.

[1] Tiffeneau and Dorlencourt, *Ann. chim.*, [8] 16, 237 (1909).

termediate dimethyl vinyl alcohol becomes stabilized through the formation of the acetate; but the carbinol isomerizes to dimethyl acetic aldehyde when it is set free by saponification.[1]

The role of the acids in these rearrangements is evidently catalytic, that is, the first phase is the formation of a "polymolecule,"[2] of carbinol and acid. Recent investigations[3] have made it probable that certain atoms, or groups of atoms, in a molecule show a selective affinity, even for solvents,[4] and, from this point of view, a *"polymolecule" should be considered as possessing an intermolecular structure.*[5] For instance, the relatively basic hydroxyl group is that component part of glycol, which should show the greatest affinity for an acid, and in their "polymolecule" the molecule of the acid should be grouped on that of the glycol, so that the acid radical is spatially as near as possible to one or to both of the hydroxyl groups.[6]

The catalytic properties of acids in these rearrangements may now be explained. In the formation of the "polymolecules" comparatively little of the free energy in the acid and the carbinol is lost, and that in the new system, which will perform the work involved in the ensuing chemical processes, is very much greater than that in the glycol alone. Further, the negative energy of the acid decreases the affinity of carbon for hydrogen,[7] which facilitates the elimination of water, and which may be an important factor in determining the decomposition of these glycols according to Type A, as the carbon of the carbinol group should be spacially nearer to the acid than that in an alkyl group.

The stability of these "polymolecules" towards water should stand in a direct relation to the relative positivity of the alkyl radicals in the glycol. Therefore, with one of these groups remaining the same, it should increase in changing the other alkyl radical from primary to secondary, and then to tertiary.[8] According to these relations, the strength, and the concentration, of the acid necessary for catalysis should decrease with

[1] Tiffeneau, *Compt. rend.*, **150**, 1118 (1910).

[2] Michael, *Ber.*, **34**, 4028 (1901); **39**, 2140, 2570; *Am. Chem. J.*, **39**, 3 (1909); **41**, 120 (1911); THIS JOURNAL, **32**, 991 (1910); **40**, 1696, 1702 (1918).

[3] Langmuir, *Met. Chem. Eng.*, **15**, 469 (1916); THIS JOURNAL, **38**, 222 (1916); **39**, 1848 (1917); Harkins, *ibid.*, **39**, 354, 541 (1917).

[4] The writer believes that the formation of "polymolecules" of solute and solvent plays an important role in the interesting phenomena described in the researches of Harkins (*loc. cit.*) on "The Structure of the Surfaces of Liquids." See Michael, *J. prakt. Chem.*, [2] **60**, 429 (1899).

[5] Michael, THIS JOURNAL, **40**, 1702, footnote (1918).

[6] In the "polymolecule" of substituted glycols and sulfuric acid, which is the acid generally used in the rearrangements, the oxygens of the sulfuryl radical should be grouped spatially as near as possible to the hydroxyls of the glycols.

[7] Michael, THIS JOURNAL, **32**, 996 (1910).

[8] Michael, *J. prakt. Chem.*, [2] **60**, 432 (1899).

increasing positivity of the alkyl groups, which appears to be the rule. And, in the direction of increasing the reaction facility, should be also the same relative relation in the alkyl radicals, since the affinity of the attached carbon for a nuclear hydrogen is decreased proportionately, while that of such hydrogens for the hydroxyl of the other carbinol group is correspondingly increased.

The course of the elimination of water from the mono- and di-alkyl α,β-glycols, in relation to their structure, may be followed from the "addition-elimination" law,[1] and the "principle of partition."[2] In agreement with the law, a tertiary carbinol loses water much more readily than a secondary of the same series, and that derivative easier than the primary.[3] Linnemann[4] found that propylene glycol may be heated with water in a sealed tube to 215°, without undergoing a change, but the addition of only a trace of hydrochloric acid to the mixture causes the formation of aldehyde. This behavior, which is so excellent a proof that the decomposition is catalytic in its mechanism, shows how much easier the secondary carbinol group parts with its hydroxyl than the primary group. According to the partition principle, however, the difference between the direct and indirect influence of methyl and hydrogen should not suffice to throw this elimination process entirely in one direction, and acetone in a small proportion should also be formed, which agrees with Eltekoff's[5] result, while Flawitzky,[6] like Linnemann, failed to detect its formation. Flawitzsky,[7] however, obtained apparently considerable methylisopropyl ketone, besides isovaleric aldehyde, in the decomposition of isopropyl glycol. This result agrees with the theory; in methyl glycol the 3 methyl hydrogens are in the unimportant fourth position to the carbon of the primary carbinol group, while, in the isopropyl derivative, there are 6 hydrogens in the very important 5 position,[8] which should give that carbinol group relatively a more secondary character than methyl does the primary radical in propylene glycol. For this reason, in the decomposition of a monoalkyl glycol, the proportion of ketone to aldehyde should increase with the relative positivity of the alkyl group, but in amount the yield of ketone should always be much less than that of aldehyde. According to the "principle of partition,"[9]

[1] Michael, *Ber.*, **34**, 4221 (1901).

[2] Michael, THIS JOURNAL, **32**, 1006 (1910).

[3] Michael and Zeidler, *Ann.*, **385**, 227 (1911).

[4] *Ann.*, **192**, 63 (1878); Krassusky, *Bull. soc. chim.*, [3] **24**, 873 (1900), found that a number of fatty glycols could be heated with water to 240° without change.

[5] *Ber.*, **11**, 990 (1878).

[6] *Bull. soc. chim.*, [2] **30**, 535 (1878).

[7] *Ber.*, **10**, 2240 (1877); **11**, 992 (1878).

[8] See "scale of combined influence," THIS JOURNAL, **32**, 999 (1910); **34**, 849 (1912); **40**, 707, 717 (1918); **41**, 398 (1919).

[9] THIS JOURNAL, **32**, 1006 (1910).

the sym. dialkyl glycols with different alkyl radicals should yield mixtures of two isomeric ketones, and, with the increasing difference between the relative positivity of the two groups, the proportion of that ketone, in which the more positive alkyl is directly joined to the carbonyl group, should increase in a direct relation to the polarity divergence of the hydrocarbon radicals.[1] Thus, theoretically sym. methyl ethyl glycol should yield a mixture of methyl propyl and diethyl ketones, and sym. methyl propyl glycol the methyl butyl and ethyl propyl derivatives, in which the first and third products should be in somewhat greater proportion. And, the relative difference in their amounts should be slightly larger in the ketones of the higher carbon series.

Pinacol ⟶ Pinacolone[2] Rearrangement in the Fatty Series.

In the tetra-alkyl glycols, the process according to (A) is structurally debarred, and the mechanism of the remarkable type rearrangement to ketones, has been the subject of an extended discussion. The first explanation was given by Erlenmeyer, senior,[3] who assumed the elimination of water to proceed with the formation of an unstable hydroxy-cyclopropane derivative, and that the ketone is then formed through the migration of the hydroxyl-hydrogen to the methylene-carbon, with the opening of the ring. The formation of intermediate ring derivatives was applied to explain other, similar rearrangements, and was investigated experimentally by Montagne,[4] who found that p-tetrachlorophenyl-pinacol yields a *pinacolone* with all the chlorine atoms still in *para* positions, whereas one of them should be in the *meta* position, if the reaction proceeds through a 4-membered ring compound. Montagne concluded that a pinacol rearrangement never takes place through the formation of an intermediate ring product, but such a comprehensive conclusion is hardly warranted by his experimental results. Erlenmeyer's hypothesis applied to wholly aromatic pinacols would lead to the intermediate formation of products with stable, 4-membered carbon rings, whose properties would preclude a transformation into a *pinacolone* under the experimental conditions. On

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[1] See *J. prakt. Chem.*, [2] 60, 432 (1899) for the polarity grouping of the alkyl radicals. The subject merits a quantitative investigation, in which the semicarbazide method (THIS JOURNAL, 41, 396 (1919)) may be used.

[2] It seems inconsistent to modify the group names of certain classes of organic compounds to conform better with their chemical structures, and leave chemically unsuitable names of other classes unchanged. For this reason, *pinacolone* is used instead of pinacoline.

[3] *Ber.*, 14, 322 (1881). See, also, Couturier, *Ann. chim.*, [6] 26, 438 (1897); Nef, *Ann.*, 318, 37 (1901); Zelinsky and Zelikow, *Ber.*, 34, 3251 (1901); Lindner, *Monatsh.*, 32, 403 (1911).

[4] *Rec. trav. chim.*, 21, 30 (1902); 24, 105 (1905); 25, 379, 411 (1906). The result was confirmed by similar experiments of Acree (*Am. Chem. J.*, 33, 180 (1905)) and by those of Meerwein (*Ann.*, 396, 210 (1913)).

the other hand, the trimethylene ring, assumed by Erlenmeyer to explain the changes with fatty pinacols, would certainly be easily ruptured between the methylene and carbinol groups, and this phase of his explanation is feasible from a chemical point of view, and a pinacolone would then be formed.

Thoerner and Zincke[1] observed the formation of aryl ethylene oxides in the decomposition of tetraphenyl and diphenyl-ditolyl pinacols by dilute acids, and that such products may be transformed into the corresponding *pinacolones* by the same reagents that serve for the first reactions. On the basis of these observations, Breuer and Zincke,[2] who had found analogous results with the hydrobenzoins, assumed the formation of substituted ethylene oxides, or less probably that of the diethylene oxides, as the primary phases in the transformations to ketones. Montagne[3] called attention to the much greater stability of the oxides than the pinacols towards the employed reagents, and expressed the opinion that definite intermediate products are not formed, but that the rearrangements occur simultaneously with the elimination of water. And, he found an experimental support to this view in Meerburg's[4] results with tetrachlorobenzopinacol and the corresponding oxide, where the reactions are of the first order, and where the transformation into *pinacolone* proceeds faster with the first compound. An extended study of the rearrangements of the α,β-glycols, and those of the corresponding aromatic iodohydrols, led Tiffeneau[5] to the conclusion that they are usually preceded by a phase of "desorganisation," with the formation of structurally unstable complexes, which reorganize to stable products, owing to the tendency of free valences to neutralize each other. According to this, quite generally accepted, view, the rearrangement of pinacol leads first to the formation of $(CH_3)_2 = C - C - (CH_3)_2$, which may change not only into *pinacolone*,

$$\begin{array}{c} | \\ -O \end{array}$$

through the migration of a methyl group, but, also, by the direct polymerization of two groups, into tetramethyl diethylene oxide. Somewhat later, Faworsky[6] showed that on heating ethylene glycol with a small proportion of conc. sulfuric acid, diethylene oxide distils off as the main product of the reaction, and that when this product is heated with the concentrated acid it gives aldehyde. He concluded, therefore, that the formation of the latter substance from glycol goes through that of di-

[1] *Ber.*, **11**, 68 (1878). Also, Klinger and Lonnes, *ibid.*, **29**, 2158 (1896).

[2] *Ann.*, **198**, 148 (1879). Erlenmeyer, Jr., *ibid.*, **316**, 84 (1901); Nef, *ibid.*, **335**, 243 (1904).

[3] *Rec. trav. chim.*, **24**, 105 (1905).

[4] *Ibid.*, **24**, 131 (1905).

[5] *Rev. gén. Sci.*, **18**, 589 (1907); *Bull. soc. chim.*, [4] **1**, 1221 (1907).

[6] *Chem. Centr.*, **1907**, I, p. 15.

ethylene oxide. Influenced by these results, Tiffeneau[1] abandoned his previous hypothesis, and assumed that dialkylene oxides are the intermediate products in these rearrangements. These theoretical conclusions are characteristic of the tendency to base explanations on rigidly mechanical conceptions of valence, and to generalize from results obtained from a single group of substances, irrespective of the fact that different affinity-energy and spatial relations may appear in other, although analogously structured groups; also, of the indifference toward taking the known correlations into consideration that exist between the main chemical processes and the structures of organic substances.[2]

The conclusions drawn by Montagne from Meerburg's results are too general. It is permissible to conclude from the greater reaction velocity of tetrachloro-benzopinacol compared to that of the oxide with acetyl chloride, that the transformation in this case does not proceed through the oxide, but not to extend the conclusion to all pinacol rearrangements, éven in the aromatic series. For instance, phenyltolyl pinacol in alcoholic solution, and in the presence of a very small amount of hydrochloric acid, passes over into the oxide at room temperature, and the *pinacolone* formation under these conditions should proceed through that of the oxide.[3] Further, it is not safe to conclude from the transformation of tetrachloro-benzopinacol being a reaction of the first order, that the relation is true for all rearrangements involving the migration of an aryl group. For instance, although benzopinacol gives a monomeric product of dehydration, the stereomeric hydrobenzoins yield dimeric products, and both the oxides are convertible into *pinacolones*.

A comparison of the reagents and the conditions for aromatic and aliphatic pinacols shows that, with one or two exceptions in the first group, the facility of rearrangement in the two series differs considerably. With the aromatic compounds, strong dehydrating agents at moderate temperatures, or concentrated solutions of strong mineral acids at higher temperatures, are required, while with the fatty substances the changes take place readily with very dil. sulfuric acid; pinacol itself rearranges even with a 5% solution of oxalic acid at 100°.[4] As such dilute solutions cannot be dehydrating in the sense of a direct affinity for water, Tiffeneau's first interpretation, which implies the existence of a strong dehydrating capacity in the reagent, is manifestly in variance with the conditions prevailing with the fatty pinacols.

    [1] *Bull. soc. chim.*, [4] 1, 1226 (1907). See Meerwein, *Ann.*, 396, 215, footnote (1913).

    [2] Michael, *J. prakt. Chem.*, [2] 60, 282, 409 (1899).

    [3] Meerwein, *Ann.*, 396, 212 (1913), showed that the oxide is not the intermediate derivative in the case of diphenyl-diphenylene glycol, and concluded that this relation holds in all pinacol rearrangements.

    [4] Vorlaender, *Ber.*, 30, 2266 (1897).

And, the later view is not tenable for the following reasons. Faworsky distilled glycol with a small amount (4%) of conc. sulfuric acid, which leads first to the formation of the acid sulfate. This energetic substance is formed in the presence of a large excess of glycol, and reacts upon it; not intramolecularly, because the alcoholic group in unchanged glycol is relatively much more basic than that in the acid sulfate, and the formation of a 3-membered ring derivative would involve a strong energetic hindrance. The second phase leads, therefore, to the formation of diethylene glycol, which condenses intramolecularly to the volatile, hexacyclic diethylene oxide. The latter compound has the property of uniting with strong sulfuric acid to form an "oxonium "salt or a "polymolecule," which on heating will strive towards conversion as far as possible into volatile products. As the stability of the hexacyclic ring has been greatly decreased through the superabundant negative energy in the added acid component, and, for the same reason, also the affinity between the hydrogens and the carbons in the methylene groups, at a temperature below the dissociation point into acid and oxide, a migration of two hydrogen atoms to adjacent methylene groups, with the rupture of the ring, takes place, and, with the volatilization of the low boiling aldehyde and the regeneration of the acid, the maximum entropy of the system under the experimental conditions is realized. Faworsky's idea, that the glycols in their conversion with loss of water into carbonyl derivatives are first changed into dialkylene oxides is founded on a misconstruction of the sulfuric acid reaction, and it is untenable for the reason that the rearrangements occur under conditions (*i. e.*, heating the pinacols with slightly acidulated water) where the formation of oxides are not only precluded, but the reverse reactions would take place. And, further, because under the conditions where glycol yields diethylene oxide, *i. e.*, distillation with strong sulfuric acid in a small proportion, pinacol gives 2,3–dimethylbutadiene almost quantitatively, and *pinacolone* in small amount only.[1]

In the previous explanations of the rearrangements in fatty pinacols, that characteristic property of tertiary carbinols to dissociate easily, through the catalytic influence of very dilute mineral acids, into alkylenes and water[2] has not been taken into consideration. That pinacol, which contains two tertiary carbinol groups, undergoes such a dehydration under the conditions of the rearrangement is shown by the simultaneous formation of 2,3-dimethylbutadiene, and that small yields of ketones from aliphatic pinacols are accompanied by the formation of such hydrocarbons in

[1] Bayer and Co., *Chem. Centr.*, **1912**, II, 1757.

[2] Butlerow, *Ann.*, **144**, 22 (1867); **189**, 75 (1877); Michael and Zeidler, *ibid.*, **385**, 228 (1911).

larger proportion.[1] Indeed, the butadiene is formed almost quantita-
tively in the distillation of pinacol with traces of salts that react acidic.[2]

The elimination phase in the pinacol rearrangement proceeds, there-
fore, according to Type C,[3] and leads in the first step to the formation
of dimethyl-isopropenyl carbinol,[4] which has the requisite affinity and
energy relation in its atoms to isomerize, with the aid of the energy in
the catalytic reagent, into *pinacolone*, and with the conversion of its free
energy into bound energy and heat to a very considerable extent.[5] For,
the Δ-hydrocarbon group of the carbinol has a large content of free energy,
then, the hydroxyl-hydrogen and the methylene-carbon atoms are in
the spatially close 1,5-position, which means a slight resistance to the
migration of the hydrogen, and, finally, the affinity of the carbinol-carbon
atom to a directly joined methyl group has been considerably lessened
through the influence of many hydrogen atoms in important positions.[6]

[1] Meerwein, *Ann.*, **396**, 227 (1913).

[2] Bayer and Co., *Chem. Centr.*, **1912**, II, 1854.

[3] See page 796.

[4] This alcohol was first prepared by Choupotsky and Mariutza (*J. Chem. Soc.
Abs.*, **48**, 727 (1890)) by heating the monochloro derivative obtained in the addition
of chlorine to tetramethyl-ethylene with water. The reaction evidently proceeds first
with the formation of tetramethyl-ethylenedichloride, which shows the characteristic
property of the tert. halides in splitting of halhydric acid very readily. The mono-
chloro alkene is, therefore, dimethyl-isopropenyl-methyl chloride, and not chloro-tetra-
methylethylene, as it is called. The corresponding carbinol was also obtained by
Courtot (*Bull. soc. chim.*, [3] **35**, 969 (1896)) in the treatment of α-2-β-trimethyl-β,γ-di-
bromo-butyric acid with potassium carbonate in a freezing mixture. To explain this
remarkable rearrangement, leading under such mild conditions to the formation of a
tertiary carbinol from a primary, and a secondary, bromo derivative, Courtot (*ibid.*,
659) assumes shifting in the positions of the bromine atom and the carboxyl group,
and compares the migration of COONa to that of COOE, in the forced abstraction
of water by P_2O_5 from ethyl phenylhydroxypivalate (Blaise and Courtot, *Compt. rend.*,
141, 724 (1905)). The rearrangement is followed by the elimination of CO_2 and HBr
to form dimethyl-isopropenyl-methyl bromide. The writer can find no analogy be-
tween the two reactions (see page 820), and believes that the first step in the rearrange-
ment lies in the interaction of β-bromine and sodium, with the consequent loss of
CO_2, to form $CH_2Br — C(CH_3) = C(CH_3)_2$, which, by addition of water, passes over
into $CH_2Br—CH(CH_3)—COH(CH_3)_2$, and then into dimethyl-isopropenyl carbinol
by the loss of HBr.

[5] *Pinacolone* represents an intramolecularly extremely well neutralized structure
(Michael, THIS JOURNAL, **32**, 1004 (1910)), which accounts for its large heat of formation
(Zoubuff, *Chem. Centr.*, **1899**, I, 516).

[6] Michael, THIS JOURNAL, **32**, 997 (1910). How readily a methyl migration may
take place is well shown by the formation of sym. tetramethyl-ethylene on warming
tert.-butyl-methyl bromide with alcoholic soda (Tissier, *Ann. chim. phys.*, [6] **29**,
362 (1893)). The affinity of the alkali for hydrobromic acid suffices in this rearrange-
ment because that of carbon for carbon in the tertiary group, and of carbon for hy-
drogen in the primary group, has been greatly diminished through the influence of the
many, spacially near, hydrogen atoms. The rearrangement is favored by the formation
of that hexylene, *i. e.*, tetramethyl ethylene, in which the positive and negative atomic

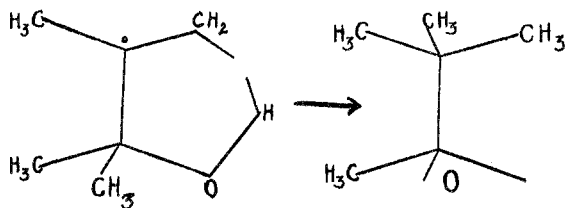The rearrangement may be represented by

Fig. 5.

No better proof can be advanced for the correctness of this intepretation than that the dimethylbutadiene is converted into *pinacolone*[1] when heated with dil. sulfuric acid, since the first step in that process must consist in the addition of a molecule of water, with formation of the Δ-carbinol.[2]

Nonexistence of the Pinacol ⟶ β-Oxide Rearrangement.

At the suggestion of Lieben,[3] Kohn[4] and Samec[5] examined the behavior of tetra-ethyl glycol, and Zumpfe[6] the corresponding propyl derivative, towards dilute sulfuric acid. Along with the corresponding Δ-hydrocarbons, products of monodehydration were obtained, which failed to show some characteristic properties of ketones, *i. e.*, they did not react with hydroxylamine or with zinc ethyl. Lieben[6] concluded from these properties that radicals larger than methyl are unable to migrate, and that, instead of *pinacolones*, β-alkylene oxides are formed by the intramolecular addition of the hydroxyl groups in the intermediate isoalkylenyl dialkyl carbinols to the Δ-carbon atoms.

forces are most symmetrically distributed and which, therefore, according to the "thermochemical law of structure" (*ibid.*, 1004), must have the largest heat of formation of the isomers. A thermochemical investigation of the alkylenes, and of other unsaturated groups of derivatives, from this point of view would be of great theoretical importance.

[1] Couturier, *Ann. chim. phys.*, [6] **26**, 493 (1892).

[2] Mariutza (*J. Chem. Soc. Abs.*, **58**, 728 (1890)) heated this carbinol with dil. sulfuric acid (1%) to 100°, and obtained a product boiling above 100°, which he believed to be a polymerization product of the dimethyl butadiene. The product undoubtedly consisted largely of *pinacolone* (106°), as any isomer of the simplest possible polymer, $C_{12}H_{20}$, would show a very much higher boiling point. Interesting is the formation of the butadiene from the Δ-carbinol when very dilute acid (0.1%) is used, which is a characteristic property of tertiary carbinols (Michael and Zeidler, *Ann.*, **385**, 227 (1911)). A systematic investigation of the relations between the concentration of the acids (see Michael and Brunel, *Am. Chem. J.*, **41**, 118 (1909); **48**, 267 (1912)), and the nature of solvents (Michael and Zeidler, *loc. cit.*) to the character and course of the reactions and to the structure of the organic substances, should yield theoretically interesting results.

[3] *Monatsh.*, **26**, 37 (1905).

[4] *Ibid.*, 111.

[5] *Ibid.*, **28**, 738 (1907).

[6] *Ibid.*, **25**, 124 (1904).

The first conclusion has been shown to be erroneous; indeed, Meerwein[1] found that ethyl instead of methyl migrates in the *pinacolonization* of unsym. dimethyl-diethylglycol, and Parry[2] that propyl and isoamyl in preference to methyl in the corresponding mixed glycols. According to the theory of the pinacol rearrangement developed in this paper, the main factors deciding the course of the transformation in the above-named glycols are: first, the relative ease of the elimination of a molecule of water from the tert. carbinol groups of different series; second, the relations in the amount of energy required to separate the migrating alkyl group, and, third, the heats of formation of the isomeric ketones that may be formed in the structural change.

It is unfortunate that the relations of the first-named factor to structure have not been determined experimentally, but they may be deduced theoretically by the application of the "addition-elimination law,"[3] which, as yet, is without an exception, and, according to which, in a series of homologous, isomeric or stereomeric compounds, the substance which is formed easier by addition from a corresponding Δ-derivative, will lose the addenda the more readily. Isobutene has been found by experiment[4] to add water, under the influence of dilute acids, more readily than any other isoalkene, and tert. butyl alcohol should lose water, therefore, more easily than any of the homologous tert. carbinols. The second of the above factors is determined by the influence of hydrogen atoms in loosening the affinity of carbon to carbon, and this influence should grow in passing from methyl to ethyl and from that radical to propyl.[5] Finally, according to the "thermochemical law of structure,"[6] that ketone among the two isomers that may be formed, will have the larger heat of formation, in which the positive alkyl radicals are to the greater extent under the influence of the negative carbonyl group. In glycols of the type $(CH_3)_2$ — COH — $COH(C_nH_{2n+1})_2$, in which n is 2 or a larger number, the elimination of water should take place, therefore, more readily from the dimethyl carbinol side of the pinacol. Further, the influence of the hydrogen atoms in loosening the affinity of carbon to carbon is greater in the larger alkyl radicals. And, finally, of the two isomeric *pinacolones* that may be formed, CH_3 — CO — $C(C_nH_{2n+1})_2CH_3$ and C_nH_{2n+1} — CO — $C(CH_3)_2C_nH_{2n+1}$, it is apparent that the positive atomic forces are grouped more symmetrically towards the negative carbonyl nucleus in the latter substances, which

[1] *Ann.*, **396**, 222 (1913); also, Romburgh and Wensnik, *C. A.*, **8**, 3297 (1914).

[2] *J. Chem. Soc.*, **107**, 108 (1915).

[3] Michael, *J. prakt. Chem.*, [2] **52**, 289 (1895); **60**, 373 (1899); *Ber.*, **34**, 4216 (1901); THIS JOURNAL, **40**, 1690 (1918).

[4] Michael and Brunel, *Am. Chem. J.*, **41**, 128 (1909); **48**, 268 (1912); Michael and Zeidler, *Ann.*, **385**, 239 (1911).

[5] See THIS JOURNAL, **34**, 850 (1912); **40**, 708 (1918); **41**, 398 (1918).

[6] Michael, THIS JOURNAL, **32**, 1004 (1910).

should have, therefore, the larger heat of formation. In ketones of the above type, therefore, all the principal energy factors coincide to favor the migration of the larger alkyl radical,[1] and the theory explains the experimental results.

In view of this relationship, it seems remarkable that derivatives of the type $(C_nH_{2n+1})_2COH$ — $COH(C_nH_{2n+1})_2$, in which n is larger than 1 and bilaterally of the same value, should give β-oxides and not *pinacolones*. Against the formation of the oxide class of compounds, it may be urged that the formation of 1,3-oxides by intramolecular addition would involve the very considerable expenditure of free energy necessary to overcome the hindrance to the formation of the 4-membered ring derivative, and that there is no experimental precedence to support such an interpretation. Further, that the supposed β-oxides are stable towards water at 200°, which is a very improbable property for a ring derivative with its affinity relations and its content in free energy. The small reactivity or indifference of ketones with the above structures towards hydroxylamine can no longer be considered crucial evidence of the absence of the keto-carbonyl group; not only are aliphatic ketones now known that are indifferent towards the reagent, but, if the products of rearrangement are keto derivatives, their slight reactivity would agree with their structures.[2] The same chemical inertia should be shown by them towards zinc ethyl, as in each case it depends on the reduction of the affinity relations, and the free energy, in the carbonyl group, by the bilateral, spatial action of large alkyl groups.[3]

The oxidation of the supposed oxide from tetraethyl glycol was carefully studied by Samec,[4] who identified diethyl-acetoacetic acid, asym. diethyl-acetone, diethyl-glycolic and diethyl-acetic acids, and isolated besides an acid, $C_{10}H_{20}O_{41}$, of unknown structure, among the products formed. This chemist, although he called attention to the correlation of these products of oxidation to a *pinacolone* constitution of the supposed oxide,[5] endeavored to explain their formation from the latter point of view,[6] but on the basis of untenable assumptions regarding the

[1] According to Richard (*Ann. chim. phys.*, [8] 21, 391 (1910)) trimethyl-tert.-butyl glycol isomerizes by the migration of the smaller methyl radical to hexamethyl acetone. A comparison of the absolutely symmetrical structure of that product with that of the other possible ketone, *i. e.*, CH_3—CO—$C(CH_3)_2C(CH_3)_3$, shows that it should have a much larger heat of formation, and this entropy factor probably outbalances that due to the larger energy factor involved in the migration of the methyl group. Theoretically, the formation of a mixture of the two *pinacolones* seems probable.
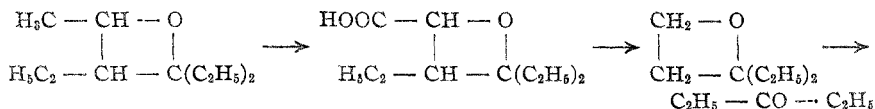
[2] Michael, THIS JOURNAL, 41, 397 (1919).

[3] *Ibid.*, 400–403.

[4] *Monatsh.*, 28, 749 (1907).

[5] *Ibid.*, 764.

[6] *Ibid.*, 762.

relation of the course of oxidation to chemical structure; for instance, he supposed the following phases of oxidation:

$$H_3C - CH - O \qquad HOOC - CH - O \qquad CH_2 - O$$
$$\qquad | \qquad | \qquad \longrightarrow \qquad | \qquad | \qquad \longrightarrow \qquad | \qquad | \qquad \longrightarrow$$
$$H_5C_2 - CH - C(C_2H_5)_2 \qquad H_5C_2 - CH - C(C_2H_5)_2 \qquad CH_2 - C(C_2H_5)_2$$
$$C_2H_5 - CO - C_2H_5$$

An oxide of the above structure must, in alkaline solution, in the primary phase, assimilate water to pass over into the β-glycol

$$CH_3 - CH(OH) - CH(C_2H_5) - COH(C_2H_5)_2,$$
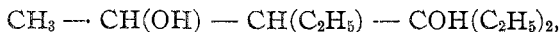
which, according to the above assumption, would be primarily oxidized by the conversion of the methyl into the carboxyl group.[1] But, the first stage must evidently consist in the oxidation of the secondary carbinol to the carbonyl group, $i.\ e.$, into

$$CH_3 - CO - COH(C_2H_5)_2 - COH(C_2H_5)_2$$

and then into

$$KOOC - CO - COH(C_2H_5)COH(C_2H_5)_2,[2]$$
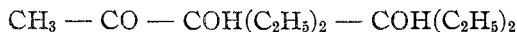
which salt should be stable towards the reagent under the conditions of the experiment. Samec's scheme of oxidation involves a series of impossible assumptions, and may be disregarded, as, even if it were accepted, it is incompatible with the formation of diethyl-acetoacetic acid. According to our present knowledge of the relation of oxidation by permanaganate to chemical structure, the *pinacolone* should pass through the following stages of oxidation:[3]

$$(C_2H_5)_3 - C - CO - CH_2 - CH_3 \longrightarrow (C_2H_5)_3 - C - CO - CO - CH_3 \longrightarrow$$
$$(C_2H_5)_3 - C - COOH \longrightarrow (C_2H_5)_2 = C(CO - CH_3)COOH.$$
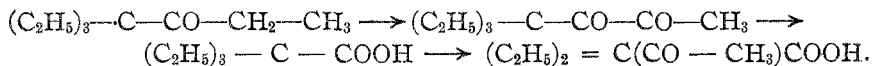
The diethyl-acetoacetate thus formed hydrolyzes readily to diethyl-acetone and diethyl acetate, and the α-hydroxy-diethyl acetate is formed by oxidation of that salt, as R. Meyer[4] has shown that the methinyl hydrogen in the salts of such tertiary acids is readily changed by permanganate into the hydroxyl group. There is, therefore, no cogent reason for accepting an oxide-structure for the product of rearrangement of any tetra-alkyl glycol, and only the pinacolone transformation is known.

Rearrangements in Aromatic α,β-Glycols.

A similar interpretation of the pinacol rearrangement in those α,β-glycols, where all the *hydrocarbyl* radicals are aromatic, would involve an o-hydrogen atom, which was theoretically improbable, as was shown

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[1] According to this assumption, if a mixture of a fatty hydrocarbon, and a sec. carbinol derived from it, are oxidized, the hydrocarbon would be attacked before the alcohol, which obviously would not be the case.

[2] Glueckmann, *Monatsh.*, **10**, 770 (1890); Wagner, *Ann.*, **298**, 284 (1897). For explanation see Michael, *J. prakt. Chem.*, [2] **60**, 356–362 (1899).

[3] Michael, *loc. cit.*

[4] *Ann.*, **219**, 234 (1883).

experimentally by Montagne.[1] The course of the structural changes proceeding in such aromatic glycols with the abstraction of water is complicated, being dependent on the character and the number of the aryl groups, but an insight into the mechanism of the rearrangements may be obtained by analysis from the affinity-energy standpoint.

When hydro- or isohydro-benzoin is boiled with a 40% solution of sulfuric acid a dehydration takes place with the formation of stereomeric tetraphenyl-diethylene oxides and of diphenyl-acetaldehyde.[2] The oxides (the so-called α-pinacolones) are dimeric,[3] and are converted, by heating higher (200°) with the above solution, or with conc. hydrochloric acid (170°), into the aldehyde; but this transformation depends on the strength of the acid, since acetic acid (170°) gives the diacetate with the oxide, and a complicated decomposition results with the iso-oxide. Benzopinacol yields *benzopinacolone* on warming with benzoyl[4] or acetyl[5] chloride, and that the transformation is due to the catalytic and dehydrating capacity of the reagents is evident from the behavior of the pinacol towards 40% sulfuric acid, or acetic anhydride, at 200°, when decomposition by heat energy into benzophenone and diphenyl carbinol alone takes place.[6] Quite a different behavior is shown by diphenyl-ditolyl pinacol; heated (160°) with 40% sulfuric, or conc. acetic acid, it yields a mixture of *pinacolone* and oxide, which, judging from analogy to the oxide from benzopinacol, is a monomeric product,[7] and the oxide separates almost quantitatively at room temperature from an alcoholic solution, which is slightly acidulated by hydrochloric acid. A factor, decidedly conducive to the dehydration through the two hydroxyl groups of these glycols (Type B), is the property of aryl radicals to favor the substitution reactivity of the hydroxyl group in aryl substituted methyl alcohols.[8] *i. e.*, to lessen the expenditure of energy required to separate it from the *hydrocarbyl* radical. They not only exert this influence to a far greater degree than any alkyl radical, but it increases in extent with the relative positive influence of the aryl group on the carbinol carbon atom.[9] Further, the aryl more than the alkyl radical is susceptible to a shifting in the molecule, since it decreases the affinity of carbon to carbon to a greater degree, and this influence, too, is augmented with increasing positivity.[3] These

[1] *Rec. trav. chim.*, **21**, 30 (1902).

[2] Breuer and Zincke, *Ber.*, **11**, 72 (1878).

[3] Auwers, *ibid.*, **24**, 1780 (1891).

[4] Linnemann, *Ann.*, **133**, 28 (1865).

[5] Thoerner and Zincke, *Ber.*, **10**, 1473 (1877).

[6] Thoerner and Zincke, *loc. cit.*

[7] Klinger and Lonnes, *Ber.*, **29**, 2158 (1896).

[8] See Meerwein, *Ann.*, **396**, 218 (1913); Tiffeneau, *Ann. chim. phys.*, [8] **10**, 325 (1907).

[9] Michael, THIS JOURNAL, **32**, 997 (1910); Meerwein, *loc. cit.*, 221–224.

relations manifest themselves, for instance, in the quantitative breaking down of benzopinacol at its melting point (204°) into benzophenone and diphenylcarbinol;[1] in the migration of the aromatic, and not the aliphatic, radical in the transformations of mixed pinacols,[2] and that the more positive of the aryl groups[3] shifts its position in the molecule in a pinacol rearrangement.[4] The intramolecular elimination of water in the sym.-diaryl-glycols tends, therefore, to proceed through the two hydroxyl groups,[5] while the loss of water in the sym. dialkyl derivatives occurs through the utilization of a nuclear hydrogen atom and a hydroxyl group; and the hindrance to the migration of the *hydrocarbyl* radical is less in the aromatic derivatives. These two factors unite to cause the characteristic difference in the behavior of the sym. diaryl- and dialkyl-α,β-glycols; the aromatic substances yielding diaryl-acetaldehydes, by aryl migration, and oxides; while the latter class of compounds gives ketones. It is evident now why the structural change takes place more readily with ditolyl-diphenyl than with tetraphenyl-glycol, and why the more positive tolyl radical in the mixed glycol is the migrating group.[4] In configurations the aryl-pinacol rearrangement may be represented by
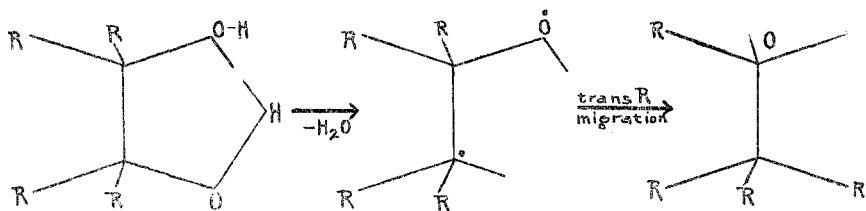
Fig. 6.

Characteristic of the aromatic glycols is the simultaneous formation of mono- or dimeric oxides. A clue to explain the different behavior of the aromatic and of the fatty glycols in this respect may be found in the stabilities of the oxides in the two series towards water. Ethylene oxide passes over into glycol when warmed with water, and the ease of conversion increases with the sym. replacement of the nuclear hydrogen by alkyl; enormously with unsym. substitution.[6] On the other hand, the replacement by aryl groups gives oxides showing a stability increasing with the number of introduced radicals; indeed, the tendency to form a monomeric oxide increases with accumulation of aryl groups, as is seen, *e. g.*, by the

[1] Thoerner and Zincke, *Ber.*, **10**, 1474 (1877).

[2] Tiffeneau, *Ann. chim. phys.*, [8] **10**, 345 (1907); Parry, *J. Chem. Soc.*, **107**, 108 (1915).

[3] Michael, *loc. cit.*

[4] Acree, *Am. Chem. J.*, **33**, 180 (1905).

[5] Meerwein, *loc. cit.*

[6] Eltekow, *Ber.*, **16**, 395 (1883); Michael, *J. prakt. Chem.*, [2] **60**, 424 (1899).

formation of such a product from tetraphenyl-glycol,[1] and dimeric oxides from the stereomeric diphenyl derivatives.[2]

In respect to the role played by the reagents in the transformations of the aromatic glycols, the behavior of the substances quoted above show that it is of a catalytic nature. Although it is only secondarily due to the hydroscopic properties of the reagents, the energy required to separate water from the two hydroxyl groups (Type B) is much greater than in the other possible two directions ((A) and (C)), as is evident from the character of the reagents necessary to effect it. From this point of view, the capability of strong acids, or of extremely energetic reagents, like the acyl chlorides, to cause the chemical changes through the considerable free energy incorporated into the reacting system by the formation of "polymolecules," will be understood, and, also, that weak acids are without action, since, although they may be decidedly hydroscopic, they are not capable of uniting in this manner with the carbinols. We may also follow the conversion of the aromatic oxides into aldehydes or ketones by treatment with the chemically strong reagents; in these cases, too, it is the added energy in the "polymolecule" of oxide and reagent that enables the chemical metamorphosis.

Rearrangements in Aryl Iodohydrols.

Apparently in a close relationship to the hydrobenzoin rearrangement, are those occurring in aromatic compounds of the type Ar.—CHOH—CH_2I, and derivatives formed by replacing one of the hydrogens in the methylene or that in the methinyl group, and both of these hydrogens, by *hydrocarbyl* radicals.[3] On treating such a derivative with mercuric oxide, or with alcoholic silver nitrate, an elimination of hydriodic acid, with a migration of the aryl group to the carbon atom which held the halogen atom takes place, and the intermediate enol structure thus formed converts itself into the corresponding aldehyde, respectively, ketone. Tiffeneau,[4] who discovered this interesting type rearrangement, discussed the possible explanations, and concluded that it takes place through the separation of the iodine and a hydrogen atom from the same carbon atom. *i. e.*, a unilateral elimination, and that the free valences in the unstable chemical system of the type Ar.—CHOH — $\overset{..}{C}$H thus formed cause a shifting of the aryl group to the Δ-carbon atom. And, he supported the explanation by showing that compounds of the type Ar.—C(OE)Alk—CHI(Alk) are converted by mercuric oxide[5] into Alk-

[1] Klinger and Lonnes, *Ber.*, 29, 2158 (1896).

[2] Auwers, *Ibid.*, 24, 1780 (1891).

[3] Tiffeneau. For the literature and a general discussion of the subject, see *Bull. soc. chim.*, [4] 1, 1205 (1907).

[4] *Ibid.*, 1207–1212.

[5] *Ibid.*, 1210.

C(OE) = C(Ar)Alk. There is a feature, however, in this class of type rearrangement which has not as yet been explained, *viz.*, that it depends on the chemical character of the reagent. It may be brought about by silver nitrate or by mercuric oxide, even with those iodohydrols whose chemical structures permit an ethylenic separation, *i. e.*, a bilateral elimination of hydriodic acid. But, with such substances, the reagent commonly used for this purpose, *i. e.*, alcoholic potash, abstracts the acid bilaterally to form ethylenic derivatives, without the occurrence of migrations; and, with the substitution of the halogen by ethoxyl, when ethylenic unsaturation is structurally precluded. This type of rearrangement depends, therefore, on specific properties in silver nitrate and in mercuric oxide, and a complete explanation must show why it is that only these reagents cause unilateral unsaturation. Mercuric oxide has the unique capacity of readily replacing hydrogen, that is directly joined to carbon, by mercury; less in evidence is this property with alcoholic silver nitrate, but the monoalkyl acetylenes yield the corresponding silver derivatives with the reagent.[1] It would seem, therefore, that the first phase in the Tiffeneau rearrangement consists in the conversion of —C(OH) — CHI — into — C(OH) — CAgI— or (C(OH) — CI)$_2$Hg, and that the formation of

the unstable radical, —C(OH)—C̈—, is due to the affinity between the metal and the halogen. It may be doubted, however, if the second phase would proceed in this manner, if a comparatively slight resistance to migration, as shown by the aryl group of Ar.—COH—, did not exist in the molecule,[2] which assists in enabling the transformation to proceed with an increase of entropy.

Benzil Rearrangement.

Although this isomerization is one of the oldest known in organic chemistry,[3] no satisfactory explanation of the change has as yet been given. According to Nef,[4] benzil adds water to form a monohydrate, which breaks down into benzophenone and dioxymethylene, C(OH$_2$); the latter product is supposed to assimilate water and give formic acid, which then adds to the carbonyl group of the ketone. A more hypothetical and impossible cycle of chemical changes is scarcely conceivable. In the first place, there is no indication of the formation of a hydrated benzil, but, even accepting its existence during the reaction, it is certain that alkali would rupture the carbon linkage between the carbonyl and the hydrated[5] group, and in forming sodium benzoate and benzoic aldehyde, a further

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[1] Behal, *Ann. chim. phys.*, [6] **15,** 408 (1888); Bruylant, *Ber.*, **8,** 410 (1875).

[2] For this reason the Tiffeneau rearrangement may not take place with the corresponding aliphatic iodohydrols.

[3] Liebig, *Ann.*, **25,** 27 (1838).

[4] *Ibid.*, **298,** 372 (1897).

[5] See page 814.

reaction could follow only on the latter product. Further, nothing would be gained by accepting the breaking up into benzophenone and dioxymethylene, as the latter complex would either decompose into water and carbon monoxide, which could not possibly react on the ketone, or isomerize to formic acid, which would immediately be converted into formate, and by no stretch of the imagination may that salt be supposed to unite with the carbonyl group of benzophenone under the conditions of the rearrangement. Tiffeneau[1] assumes the addition of a molecule of alkali to each of the carbonyl groups, then an elimination of water from the addition product, and isomerization of the dipotassium oxo-ethylene derivative thus formed to dipotassium benzilate. Against this explanation it may be urged that there is no experimental evidence, nor is it probable, that benzil is capable of adding two molecules of alkali, or that benzilic acid forms a dibasic salt. Further, that our knowledge of the properties of the alkylene oxides indicates that Tiffeneau's hypothetical oxide, instead of being formed, would add water under the conditions of the rearrangement; and, even accepting its formation, the reason for and the mechanism of the process are no clearer than before.

Schroeter[2] supposes the primary formation of C_6H_5—C(OK)OH—CO—C_6H_5, which breaks up into C_6H_5—C̈—CO—C_6H_5 and KO—OH, then a rearrangement of the first complex into diphenylketene, which reacts on the metallic hyperoxide to form potassium benzilate. This construction is supposed to find an experimental support in the decomposition of azibenzil into nitrogen and diphenylketene.[3]

The analogy between the breaking down of the assumed benzil-alkali addition product and the azi derivative is only superficial. The azi group is distinguished by the readiness with which it separates from carbon, whereby the very considerable amount of free energy in the nitrogen group is, in passing over into free nitrogen, practically converted into bound energy and heat.[3] On the other hand, the substance C_6H_5—C(OK)OH—CO—C_6H_5, whose formation is due to the strive of the free negative energy in the carbonyl group and the positive of the alkali towards neutralization, and proceeds with the considerable conversion of the free energy of the system into bound energy and heat, would, in breaking up into C_6H_5—C̈—CO—C_6H_5 and KO—OH, form a system far richer in free energy; i. e., there would be a spontaneous degradation of entropy, which is not possible. Indeed, the extremely strong capacity of the divalent carbon atom to unite with oxygen, and the strong oxidizing power of potassium hyperoxide, makes the reverse reaction much more probable; that is, such a benzil addition product, instead of splitting

[1] Rev. gén. Sci., 1907, 585.

[2] Ber., 42, 2345 (1911).

[3] Michael, THIS JOURNAL, 32, 991 (1910); J. prakt. Chem., [2] 68, 487 (1903).

up, would be formed from Schroeter's hypothetical substance and potassium hyperoxide. Finally, diphenylketene has not been converted into benzilic acid, but with alcohol, which is present in the usual preparation of the benzilate from benzil, it passes over very readily into diphenylacetic ester, which compound, or the corresponding alkali salt, is not formed in the rearrangement.

The affinity of the carbon atoms of the carbonyl groups in benzil for each other has been greatly reduced by the attached oxygen atoms,[1] and the compound is easily ruptured in many of its reactions at that point. For instance, hydrocyanic acid possesses the catalytic property of causing certain organic substances to decompose at moderate temperatures, with the assimilation of water or alcohol. Benzil in alcoholic solution with nascent hydrocyanic acid at room temperature, or at a somewhat higher temperature with the aqueous acid, is split between the carbonyl groups and gives benzoic aldehyde and ester.[2] And, when it is treated with a strong soda solution and potassium cyanide, which mixture shares the catalytic properties of the acid, it is decomposed at ordinary temperature into benzoate and benzoic aldehyde.[3] That benzil shows such a contrast in its stability towards water and prussic acid, or soda and the cyanide, and on heating with alcoholic, or very concentrated aqueous, caustic potash, is due to the conversion of the CO — CO group under the latter conditions into —C(OK)OH — CO—.[4] Since the alkali practically neutralizes the negative energy in the carbonyl groups, it greatly increases the amount of energy required to separate the carbon atoms in these groups, while it decreases to a corresponding extent that necessary to rupture the carbon atom of the C(OK)OH from the phenyl group.[5] This change in the affinity relations permits the reaction to proceed in a different direction, and with a far greater entropy increase, as, instead of forming a mixture of the neutral benzoic aldehyde and a salt of the weak benzoic acid (K, 6.10^{-5}), the system may now completely convert itself, by the trans-migration of phenyl and hydrogen, into a salt of the relatively strong benzilic acid (K, 92.10^{-5}),[6] and the extent of the

[1] Michael, THIS JOURNAL, 32, 996 (1910).

[2] Michael and Palmer, Am. Chem. J., 7, 190 (1885).

[3] Jourdan, Ber., 16, 659 (1883).

[4] The violet coloration on treating benzil with alcoholic potash is undoubtedly due to the formation of an addition product; on heating the solution it disappears with the formation of benzilate and benzoate.

[5] Michael, THIS JOURNAL, 32, 996–998 (1910). The influence of strong, positive chemical energy in decreasing the affinity of carbon for carbon is a subject that deserves far more attention in chemical theory than it has received, and a systematic experimental investigation of the subject would certainly yield results of great theoretical interest.

[6] The spatial proximity (1,5) of the carbinol hydroxyl-oxygen and the acidic hydrogen in benzilic acid explains its large affinity constant (Michael, THIS JOURNAL, 34, 849 (1912); 40, 705 (1918).

neutralization of the great positive energy still remaining in the alkali is the dominating factor in the conversion of the free energy of the system into bound energy and heat. The isomerization of the benzil-alkali product may be represented by
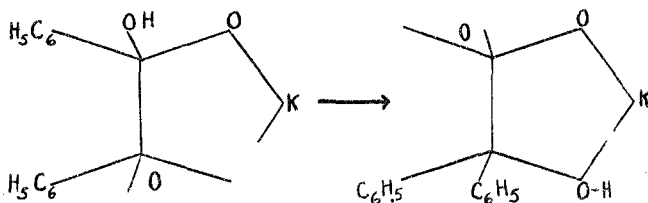

Fig. 7.

This interpretation explains why benzilate is formed almost quantitatively, when benzil is fluxed with a large excess of alkali and but little water,[1] while with alcoholic potash more or less benzoate is formed at the same time. The alkali-benzil addition product cannot be very stable towards water, but must be hydrolyzed into benzil and alkali in a direct proportion to the amount of water present, and increase in its stability proportionately to the concentration of alkali. Towards alcohol such an easily hydrolyzed salt must be more stable than towards water, and the amount of alkali-addition compound must stand in a direct ratio to the concentration of the alcoholate and of the alcohol. In the decomposition of benzil under these varying conditions, the proportion formed of benzilate to benzoate must depend, therefore, on that of addition-product to benzil in the reacting mixtures.

Intermediate Products in Rearrangements.

The question of the possible existence of such substances in type rearrangements, as are assumed in some of the above reaction schemes, has been the subject of considerable discussion, and will be briefly considered at this place from the energy-spatial standpoint.[2]

[1] E. Fischer, *Ber.*, **14**, 326, footnote (1881).

[2] The spatial factor in intramolecular rearrangements has not hitherto been taken into account; not even in other kinds of intramolecular reactions has it received nearly the consideration it merits. Its great importance is evident, when one considers that the bound energy acting through space between two atoms, stands, *cet. par.*, in an inverse ratio to this distance (THIS JOURNAL, **32**, 999 (1910)).

A number of mechanical explanations of the rearrangement phenomenon have been given which are in direct opposition to the energy-spatial atomic relations, and which, for this reason, cannot be considered tenable. For instance, Lapworth (*J. Chem. Soc.*, **73**, 448 (1898)) explains the change of $X—C_\alpha—C_\beta = C_\gamma—Y$ into $Y—C_\alpha—C_\beta = C_\gamma—X$, by supposing C_α to bend towards C_β, so that the single union between them passes over into double linkage, and by so doing X approaches C_γ so closely that it may pass over to it, along with the change of the double linkage between C_β and C_γ into single. A repetition of this process between C_γ and C_α is supposed to explain

The unstable structure in (A)[1] in the rearrangement of glycol may pass over, by the gyration of the methylene group, into vinyl carbinol (1), which in itself would not require a considerable expenditure of its free energy, but, along with the isomerization, a further conversion of free energy into bound energy and heat occurs at all the atoms, although mainly at the carbon atoms with the formation of the so-called double linkage.[2] The conversion of the unstable structure into aldehyde (2) may proceed through that of vinyl carbinol (1), but that isomerization evidently depends upon the affinity of the methylene carbon for the migrating hydrogen. This relation may be so reduced by substituting the methylene hydrogens by strongly positive, or by negative radicals,[3] that intermediate products of the vinol type become stable under ordinary conditions. The aryl group exerts such a positive influence, which explains the existence of $(C_6H_5)_2—C=C(OH)C_6H_5$ in a free state,[4] and, also, that this substance, and not the isomeric keto derivative, is obtained in the elimination of water from triphenylglycol.[5]

The intermediate structure in type (B)[6] evidently parts with much of its free energy in its transformation into aldehyde, ethylene or diethylene oxide; and, also, that in (C)[6] in becoming a ketone; in the latter case, not only in the expenditure of energy involved in the migration of R and H, but because the free energy at the Δ-carbons is largely converted into bound energy and heat. It is evident that all these intermediate structures loose considerable of their free energy in passing over into the more stable forms, and, with this dynamic loss, the quality of the remaining rearrangements of this type, since X and Y have exchanged places in the molecule.

The explanation is founded on the disproven van't Hoff conception of double linkage (see THIS JOURNAL, 40, 705, 1674 (1918)); moreover, a considerable expenditure of energy would be required to bring the saturated groups centered about C_α and then about C_γ into double union which occurs without any apparent connection to the free energy in the system. Further, the fruitless chase of X for Y, involving the overcoming of great energetic hindrances, is unnecessary, as these atoms or group of atoms are not, as represented in the Lapworth diagram, separated as far as possible in the molecule, but are in the spatially closest positions (1,5), without being in direct union. And, after all these improbable assumptions, we are no nearer to an explanation than before, as no reason has been given why they should occur. This criticism of the Lapworth hypothesis may be extended to many other attempts at explanations of organic changes that are based on the current mechanical conception of the valence phenomenon (see THIS JOURNAL, 32, 1007 (1910)).

[1] See page 794.

[2] Michael, THIS JOURNAL, 40, 703 (1918).

[3] Michael, ibid., 32, 995–998 (1910); Ann., 363, 23 (1918).

[4] Biltz, Ann., 296, 242 (1898); Ber., 32, 650 (1899); see Michael, Ann., 363, 23 (1907).

[5] Tiffeneau, Compt. rend., 146, 29 (1908).

[6] See page 796.

free energy, *i. e.*, the affinity values of the atoms or groups that may determine a further change, usually fall off in the same direction. For instance, it is obvious, that the unstable structure in (B) possesses, in the amount and nature of the free energy in its Δ-oxygen and its Δ-carbon, a greater capacity to isomerize into an aldehyde or a ketone, than the corresponding ethylene oxide does, and that a further decrease, but to a less degree, must be shown by diethylene oxide. It is this quantity and quality of the free energy in the intermediate form in (B) that enables the direct rearrangement, which, to bring about with the oxides, can be done only with the aid of extraneous chemical energy in a more or less considerable amount.[1]

The experimental conditions in the rearrangements of the α,β-glycols are not favorable to the isolation of intermediate structures, but this is by no means impossible in some other classes of rearrangements.

Phenyl isonitrile isomerizes to the nitrile at a moderately high temperature,[2] and, if it were formed in reactions only proceeding at a higher temperature, the isonitrile would not be known. The actual temperature, however, to which a chemical structure is exposed at the moment of its formation is not the outward, measured by a thermometer, but the inward—"the internal maximum heat"[3]—existing before the heat energy generated by the interacting molecules becomes dissipated through the mass, and which must be considerably higher. Evidently, what are considered unstable chemical structures in some cases are so only in a relative sense, since chemical affinity is dependent on heat energy, and there can be no doubt that some of the intermediate, under the ordinary conditions of experimentation, unstable forms may be isolated, if the "internal maximum heat" may be controlled, and the reaction would take place under such conditions. For instance, silver enol-aceto-bromo-amide, answering to its affinity relations and its stereo structure, is a very unstable product,[4] and it is by no means impossible that, with the highly favorable energetic-spatial relations existing in the halogen and metal for interaction,[5] the decomposition may be conducted at a sufficiently low temperature to give stability to the assumed intermediate product, $CH_3 — C(O)N$.

Unilateral Elimination and Rearrangement.

In several of the reactions considered above a one-sided elimination of a group of atoms, *i. e.*, separation from a single carbon atom, is assumed. As the theoretical bearing of this important subject has been obscured by

[1] See page 795.
[2] Weith, *Ber.*, **6**, 213 (1873).
[3] Wohl, *Ber.*, **40**, 2290 (1907); Michael, THIS JOURNAL, **32**, 992 (1910).
[4] Mauguin, *Ann. chim. phys.*, [8] **22**, 313 (1911).
[5] See page 791.

untenable speculations,[1] it, too, will be considered briefly from the stand-point of the affinity-energy relations.

When hydrobromic acid is removed from ethyl bromide by means of an alkali, a bilateral elimination of its components takes place for the following reasons: the affinity of the relatively negative hydroxyl group of the alkali is greater for the hydrogen of the methyl group, because they are relatively positive to those in the CH_2Br radical, but the main factor is that ethylene must have much less free energy, $i.\ e.$, a larger heat of formation, than the isomeric ethylidene would have. This important energetic relation follows from the sphere-segment theory,[2] since in the formation of ethylene a further segmentation of the carbon atoms occurs, whereby a considerable amount of their free energy is converted into bound energy and heat,[3] whereas in that to ethylidene, a further carbon segmentation is structurally excluded. These energetic relations are expressed in the following sphere-segment structures:[4]

Fig. 8.

What are the structural and energy relations in an organic molecule that favor the existence of unilaterally unsaturated substances, and the unilateral elimination of a component part? It is obvious that such an unsaturated compound, with an enormous inherent motive power, than is actuated by a large content in free energy centered at a single carbon atom, should show at that point a great capacity for intermolecular carbon polymerization or for inducing an intramolecular rearrangement; in either case with a large increase in the entropy of the system. Any chemical change in the structure of a complex containing a unilaterally

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[1] Nef, *Ann.*, **298**, 202 (1897); **309**, 126 (1899); **318**, 1, 137 (1901); THIS JOURNAL, **26**, 1549 (1904); **30**, 645 (1908). Nef at first assumed ethylenic dissociation only, but this view led to conclusions that were irreconcilable with the most common chemical facts; *e. g.*, the same product of reaction should be formed with isomeric primary, secondary and tertiary halides (Michael, *Am. Chem. J.*, **25**, 427–30 (1901)). There is no connection between the chemical nature and the structures of the substances and the course of the reactions in Nef's views, and his explanations mostly halt after the results of experimentation; that is, in stating to accord with them, that the process proceeds through ethylenic or methylenic dissociation, or in both directions (see Michael, *J. prakt. Chem.*, [2] **60**, 471–479 (1899)). Moreover, many assumptions involved in his explanations are obviously impossible.

[2] THIS JOURNAL, **40**, 705, 1674 (1918).

[3] *Ibid.*, **40**, 705 (1918).

[4] The relative proportion of the bound energy between the carbon atoms is represented by the extent of the segmentations and the spheres represent the "co-volumes" or "vibratory volumes" of the atoms.

Δ-carbon atom, that diminishes the affinity of that Δ-carbon for itself, will decrease its tendency to react by intermolecular carbon polymerization. Such an influence is exerted by positive, and by negative, radicals; especially when they are in direct union with the Δ-carbon, and to an extent proportionate to the magnitude of the influence.[1] On the other hand, any change that diminishes the affinity of the unilaterally Δ-carbon for those atoms, or groups of atoms, in the molecule, that by migrating to it would form a more stable isomer, will decrease the tendency towards an intramolecular rearrangement to a corresponding degree. And the combined influence of both these factors may enable the unilaterally Δ-structure to exist in a free state.[2] The amount of free energy at the Δ-carbon atom of ethylidene, and its affinity for itself and for hydrogen, are evidently too developed for the stability of such a structure, and it must either spontaneously polymerize to 2,3-butylene or isomerize to ethylene. It is a well-known fact that aryl radicals exert an extremely strong positive influence on any atom joined directly to them and that they, therefore, reduce the affinity of such atoms for each other very materially. The separate existence of fully substituted, aryl derivations of methyl, and of similarly constituted nitrogen products, are, therefore, interesting confirmations of the theory.[3] And, since negative radicals also tend to inhibit carbon polymerization,[4] there is no theoretical reason why a system like $C(NO_2)_3$, or perhaps one in which nitroxyl is replaced by a less strong negative radical, should not have a free existence.

As a further illustration, the formation of phenylisonitrile from aniline and chloroform will be analyzed, where the motive power is the affinity of the alkali for the halhydric acid, and which proceeds through the following phases:

$$C_6H_5 - NHCHCl_2 \xrightarrow{-HCl} C_6H_5 - N = CHCl \xrightarrow{-HCl} C_6H_5 - N = \ddot{C}.[5]$$
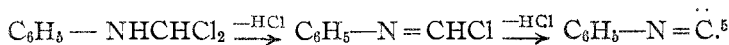
The large free energy content in the isonitrile[6] manifests itself in its chemical properties, and the unilaterally, unsaturated compound is stable under ordinary conditions for the following reasons: A carbon polymeriza-

[1] THIS JOURNAL, 32, 996 (1910).

[2] J. prakt. Chem., [2] 60, 298, 478 (1899).

[3] THIS JOURNAL, 32, 997 (1910).

[4] Ibid., 996.

[5] It is interesting to note that Gautier (Ann. chim. phys., [4] 17, 209 (1869)), who discovered the aliphatic carbylamines, assigned them the divalent carbon structure.

[6] This reaction proceeds exothermally with a large increase in the entropy of the system; the increase of free energy in the isonitrile is slight in comparison to the decrease accompanying the neutralization of the hydrochloric acid by the base. The formation of the isonitrile, energetically the extropic (THIS JOURNAL, 40, 1707 (1918)) part of the reaction, is forced, as through it lies the only way that the system can realize the condition of maximum entropy. Similar energetic relations are frequent in organic reactions.

tion to C_6H_5—$N = C = C = N$—C_6H_5 appears possible from the valence viewpoint, but its formation is enjoined by the reduction of the affinity between the Δ-carbon atoms by the negative nitrogen radical; similarly, an oxygen atom prevents the carbon polymerization of carbon monoxide. Another valence possibility would be realized in a carbon-nitrogen polymerization, to yield a 4- or a 6-membered ring derivative containing divalent carbons. The spontaneous formation of tetracyclic ring compounds by polymerization is of rare occurrence; it takes place only when a very great difference exists in the polarity of the Δ-atoms, as is the case in $CH_2 = C(COOE)_2$, which is also an essential condition for a facile polymerization to a hexacylic derivative.[1] Further, the production of either of these ring derivatives is not favored by the comparatively weak affinity relations between the unsaturated carbon and nitrogen atoms.

Generally speaking, there is theoretically no energetic obstacle to the chemical breaking up of an organic substance by unilateral elimination, and it is of rare occurrence only because, for reasons given above for the formation of ethylene from ethyl bromide, a greater entropy increase goes along with the bilateral procedure. Such a one-sided unsaturation may be brought about, however, by so changing the structure of a substance, that no two of the groups in direct union contain atoms or groups of atoms that show more than a very slight affinity for each other, or for the reagent used in the reaction; while conditions favorable for the separation of a component part exist in a group with a single carbon atom. And, the relative ease with which such a unilateral elimination takes place will depend on the affinity of the reagent for the removed part, and on the expenditure of energy essential for the elimination, which, evidently, is a constitutive factor.

For instance, benzyl bromide reacts with alcoholic potash by substitution and yields benzyl ethyl ether, but, with the introduction of an o-, or a p-nitro group, the reaction proceeds partially with the formation of dinitro stilbenes.[2] Nitroxyl is the strongest known negative radical, and in these positions greatly reduces the affinity of the carbon in the CH_2Br group for the hydrogens and also for the halogen. This influence, in decreasing the energetic hindrance to the elimination of halhydric acid, evidently favors its separation from the molecule, but the negative influence on the carbon atom does not suffice to prevent the polymerization of two molecules of the intermediate products, $C_6H_4(NO_2)\overset{..}{C}H$, to the stilbene derivatives. It is theoretically not impossible, however, that a greater accumulation of negative influence, perhaps that of two nitro-

[1] Michael, *J. prakt. Chem.*, [2] **60**, 437–443 (1899).

[2] Strakosch, *Ber.*, **6**, 328 (1873); Bischoff, *ibid.*, **21**, 2072 (1888); Elbs and Bauer, *J. prakt. Chem.*, [2] **34**, 344 (1886).

groups in *ortho* positions, may inhibit carbon polymerization sufficiently to give stability to the intermediate methylene derivative.   Or, the conversion of C_6H_5—CHOH—$C(CH_3)_2$—COOE, into C_6H_5—C(COOE) $=C(CH_3)_2$ by dehydration with phosphorus pentoxide.[1]   Methyl alcohol is not eliminated in this reaction, owing to the very considerable expense of energy required to separate the methyl group from the carbon atom, while the unilateral elimination of water is facilitated by the phenyl and the carbethoxyl group in decreasing the affinity between the carbinol-carbon and the hydrogen and hydroxyl.   The great reservoir of free energy at the Δ-carbon in the intermediate structure, C_6H_5 — $\overset{..}{C}$ — $C(CH_3)_2$ — COOE, induces a rearrangement, in which the carbethoxyl, and not one of the methyl groups, migrates, because the energy required to separate the first group from carbon is less, and, because the heat of formation of the substance thus formed is probably greater than that of the isomeric ester.

The subject of organic rearrangement is far too comprehensive for treatment in a single paper, but it is believed that the analysis of typical reactions given above will suffice to enable the application of the affinity-energy-spatial viewpoint to other chemical transformations of this nature without difficulty.

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THE ORIGIN OF THE HUMIN FORMED BY THE ACID HYDROLYSIS OF PROTEINS. V.[2]

BY ROSS AIKEN GORTNER AND GEORGE E. HOLM.

Our earlier contributions to the subject of humin formation[3] have led us to draw the conclusion that the formation of the black acid-insoluble humin on protein hydrolysis is due almost wholly to the interaction of tryptophane with some aldehyde or ketone and that no other known amino acid enters into the reaction to any appreciable extent.   All of our earlier data have, however, involved the use of proteins, some of which were known to contain tryptophane, others from which this amino acid is supposed to be absent.   By the addition of tryptophane to the latter, humin formation was markedly increased and we were unable to find any other group of compounds which would cause this increase excepting those con-

[1] Blaise and Courtot, *Bull. soc. chim.*, [3] **35,** 589 (1906).

[2] Published with the approval of the Director as Paper No. 193, Journal Series of the Minnesota Agricultural Experiment Station.

[3] THIS JOURNAL, 37, 1630–1636 (1915); *J. Biol. Chem.*, **26,** 177–204 (1916); THIS JOURNAL, 39, 2477–2501 (1917); *ibid.*, **42,** 632 (1920).