concentrations of the substances involved.

From van't Hoff's equation

$$\log K_2 - \log K_1 = \frac{q}{2}\left(\frac{1}{T_1} - \frac{1}{T_2}\right)$$

Where K_1 and K_2 are the equilibrium constants at the temperatures T_1 and T_2, T_2 being the higher, and q the heat of formation of A. Since q is positive[1] K_2 must be larger than K_1 or less of the compound is produced at a low temperature than at a higher one. It seems probable, then, that these compounds cannot be produced in a reasonably pure state by cooling their solutions to a low temperature.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS.]

MOLECULAR REARRANGEMENTS OF CARBON COMPOUNDS.[2]

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Table of Contents.

1. Types of Chemical Reaction.

In the study of molecular rearrangements of carbon compounds, two types of chemical reactions are noted; the reversible and non-reversible.[3] Tautomerism furnishes many examples of molecular rearrangements of the reversible type. Wislicenus showed, in the case of formylphenylacetic ester,[4] that in certain solvents an equilibrium between the two isomeric forms is established, which equilibrium is dependent upon temperature, concentration, and the nature of the solvent. Molecular rearrangements of the non-reversible type are illustrated by the change of Δ^2 unsaturated acids into their Δ^1 isomers by boiling with alkalis.

A further study of reversible and non-reversible molecular rearrangements shows that certain rearrangements occur when atoms are added to or substracted from the original molecule, while in many other cases the rearrangement consists only in the readjustment of the atoms already present in the molecule. Molecular rearrangements of the former class

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[1] Contrast Hildebrand and Glascock, THIS JOURNAL, 31, 26 (1909).

[2] Presented in abstract at the Boston meeting of the American Chemical Society. From the author's thesis in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Illinois.

[3] For a definition of these terms see Nernst, Theoretische Chemie, Sechste Auflage, especially pages 668-70.

[4] Wislicenus, *Ann.*, 306, 322 (1899); 300, 206.

will be termed rearrangements with reaction while those of the latter class will be called true rearrangements or rearrangements without reaction. Tautomeric changes illustrate true rearrangements of the reversible type, while the change of Δ^2 unsaturated acids to their Δ^1 isomers furnish illustrations of non-reversible rearrangements of this class. The historic rearrangement of pinacone to pinacolin by the elimination of water illustrates a rearrangement with reaction. The following discussion will deal mainly with true rearrangements of the non-reversible type.

2. Formation and Stability of Compounds that Rearrange.

It has often been suggested by chemists that molecular rearrangements occur in the direction to produce a more stable substance. Before this idea can be developed it is necessary to consider carefully the conditions under which compounds rearrange, as well as the nature of the compounds. Nernst[1] states: "The fact that reaction velocity in chemical systems is usually extraordinarily small, no matter how far removed from the point of equilibrium, is of the very greatest importance for our knowledge of chemical compounds. Probably nine-tenths, or rather ninety-nine one hundredths, of all organic compounds would never have seen the light of day if they had proceeded to their stable conditions with greater velocity. The many polymeric hydrocarbons of the formula C_nH_n could not exist at the same time if they all tended to go at once to the system of greatest stability corresponding to the formula C_nH_n. In the sense of the preceding, *organic chemistry is peculiarly the region of unstable compounds*, and these either go over to a more stable form very slowly in a measurable time or else not at all. In most cases heat only accelerates a reaction—whether a decomposition or a union—which would take place spontaneously, though, to be sure, perhaps only during the lapse of, say, a thousand years."

Baeyer, in his work upon terephthalic and phthalic acids, furnishes the experimental part to Nernst's discussion. Terephthalic acid upon reduction in the cold with sodium amalgam, in the presence of carbon dioxide to remove the hydroxyl ion, gives $\Delta^{2,5}$-dihydroterephthalic acid. This acid rearranges to the $\Delta^{1,5}$ isomer upon warming with water. The $\Delta^{1,5}$ acid, when boiled in the presence of hydroxyl ions, gives the $\Delta^{1,4}$-dihydroterephthalic acid. Baeyer concluded that the $\Delta^{2,5}$-dihydro acid is the most unstable, while the $\Delta^{1,4}$ isomer is the most stable. Using a more vigorous reducing agent, namely sodium amalgam in the absence of carbon dioxide gas, he obtained no $\Delta^{2,5}$-dihydroterephthalic acid, but more stable products. On the other hand, the reduction of phthalic acid at a higher temperature by sodium amalgam in the absence of carbon dioxide gives the most stable tetrahydrophthalic acid. No unstable

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[1] Nernst, Theoretical Chemistry. Translation of revised 4th German edition, 672.

intermediate dihydro or more unstable isomeric tetrahydro acids could be formed under these conditions, so that molecular rearrangements are not possible, because the product first formed by the reduction is the most stable. Thus the conditions under which compounds must be formed which undergo true molecular rearrangements of the non-reversible type, become evident, namely that the reagents used at the time of formation as well as the speed of the reaction must be such that unstable compounds are produced.

3. Catalysis of Speed of True Rearrangements of the Non-reversible Type.

According to Nernst the unstable compounds, considered above, may be going over to a more stable state very slowly in a measurable time or else not at all. It is evident that true rearrangements of the non-reversible type occur in unstable compounds which go, spontaneously, to a more stable state. In the case of the rearrangement of $\Delta^{2,5}$-dihydroterephthalic acid to the $\Delta^{1,5}$ isomer, simply heating with water caused the reaction to be complete in a short time. In many other cases heat is the only thing necessary to complete the rearrangement in a short time. The $\Delta^{1,5}$-dihydroterephthalic acid rearranged to the $\Delta^{1,4}$ isomer when boiled with hydroxyl ions. Thus it appears that the reagents used in true rearrangements of the non-reversible type are catalysts to the speed of the rearrangement and in their presence reactions which might take thousands of years are completed in a few minutes. Goldschmidt and Reinders[1] have proved this to be the case for the change of diazoaminobenzene into aminoazobenzene. A thorough study of the catalytic influence of the reagents added to hasten true rearrangements of the non-reversible type will be made in the near future.

4. A Correlation of True Molecular Rearrangements of Acids and Bases, Belonging to the Non-reversible Type, With the Free Energy of Ionization.

Under 2 it was shown that the reaction velocity and stability were of fundamental importance in the study of rearrangements of this type, so that some measure of these factors must be found. Reaction velocity is readily determined by the amount of the substance changed in a given time, but a measure of stability is not so readily obtained. The term stability is frequently used in a vague way. It has an exact meaning only when the conditions are specified, as will be seen in the following: The above quotation from Nernst makes it evident that when a reaction takes place *spontaneously* (or may so take place if sufficient time is given) the initial substance is unstable with respect to the final and hence there is a decrease in free energy during the change. As stated above, in true rearrangements of the non-reversible type, the initial substance is slowly changing into its isomer even in the absence of a catalyzer. Thus the initial substance in such a rearrangement must be unstable with respect

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[1] *Ber.*, **29**, 1369, 1899 (1896).

to the final substance. Yet, as stated in the quotation from Nernst, the final substance may be unstable with respect to other substances as, for example, to the elements carbon, hydrogen, and oxygen. Hence in the previous discussion stability toward rearrangements is meant whenever the term is used.

In seeking a criterion of stability in true rearrangements of the non-reversible type, the logarithm of the ionization constant of acids and bases has been chosen. From the second law of thermodynamics, the expression, $A = RTlnK$, is obtained, in which

A is the free energy of ionization,
R is the gas constant,
T is the absolute temperature, and
K is the ionization constant.

The free energy of ionization of acids and bases is "the change in free energy" as expressed by the reaction $HA \rightleftarrows H^+ + A^-$ for acids and $ROH \rightleftarrows R^+ + OH^-$ for bases when the initial and final substances are at unit concentration. Therefore, the above expression gives a measure of the free energy of ionization in terms of the ionization constant and shows that the free energy of ionization is directly proportional to the natural logarithm of the ionization constant. Since that acid is most stable toward ionization which possesses the smallest amount of free energy of ionization, it is evident that when one acid has a smaller ionization constant than another the change in the free energy of ionization is smaller and its stability with respect to ionization is greater. Therefore to determine the relative stabilities of two acids in terms of the free energy of ionization, we need only to compare the logarithms of their ionization constants.

In the following table examples of true rearrangements of the non-reversible type are given. The Briggsian logarithm of the ionization constant of each acid or base that undergoes the rearrangement is given in column 6, and that of the isomer resulting from the rearrangement is given in column 7. From this table it is evident that the free energy of ionization of the initial substance is greater than that of the final substance and that during the rearrangement there has been a decrease in free energy. The final substance is, therefore, more stable toward ionization than the initial substance. As stated above, the final substance in a rearrangement of this type must be the more stable toward rearrangement, so that that acid or base is most stable toward rearrangement which is also most stable toward ionization as Table I shows. Hence, *the final (stable) substance in a series of true rearrangements of the non-reversible type has a smaller ionization constant (or free energy of ionization) and the logarithm of the ionization constant may therefore be taken as a criterion of stability in these rearrangements.*

The meaning of the classes referred to in Table I will be explained in the final section of this article.

TABLE I.

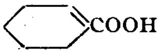
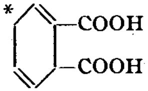
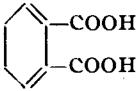
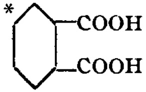
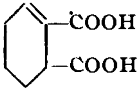
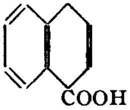
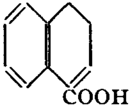
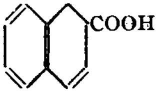
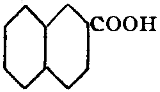
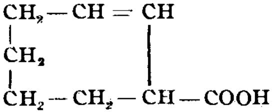
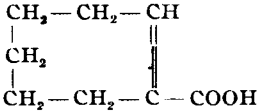
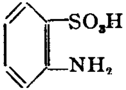
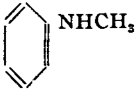
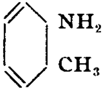
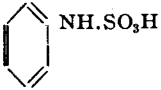
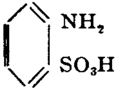
	True molecular rearrangements (non-reversible).			Ionization constants at 25°.			
				K.		Log. $K \times 10^5$.	
Class.	Before.	After.	Catalyzer.	Before.	After.	Before.	After.
1	$CH_3.CH_2.CH{=}CH.CH_2COOH$/ Δ^2 Hexenoic acid (Dihydrosorbic acid)	$CH_3.CH_2.CH_2.CH{=}CH.COOH$ Δ^1 Hexenoic acid	OH^-	2.64×10^{-5}	1.89×10^{-5}	0.423	0.2775
	$CH_3.CH{=}CH.CH_2COOH$ Δ^2 Pentenoic acid	$CH_3.CH_2.CH{=}CHCOOH$ Δ^1 Pentenoic acid	OH^-	3.35×10^{-5}	1.48×10^{-5}	0.526	0.172
	 Δ^2 Tetrahydrobenzoic acid	 Δ^1 Tetrahydrobenzoic acid	OH^-	3.05×10^{-5}	2.21×10^{-5}	0.478	0.344
	 $\Delta^{2,5}$ Dihydrophthalic acid	 $\Delta^{2,6}$ Dihydrophthalic acid	OH^-	2.46×10^{-4}	1.65×10^{-4}	1.392	1.218
2	 Δ^1 Tetrahydrophthalic acid	 Δ^2 Tetrahydrophthalic acid	OH^-	5.9×10^{-4}	7.6×10^{-5}	1.772	0.882
	 Δ^2 Dihydro-α-naphthylic acid	 Δ^1 Dihydro-α-naphthylic acid	OH^-	1.14×10^{-4}	8.1×10^{-5}	1.058	0.909
	 Δ^2 Dihydro-β-naphthylic acid	 Δ^1 Dihydro-β-naphthylic acid	OH^-	5.9×10^{-5}	2.9×10^{-5}	0.772	0.463

Table I—(*Continued.*)

Class.	True molecular rearrangement (non-reversible). Before.	After.	Catalyzer.	Ionization constants at 25°. K. Before.	After.	Log. $K \times 10^5$. Before.	After.
	 Δ^2 Cycloheptene carboxylic acid	 Δ^1 Cycloheptene carboxylic acid	OH^-	2.7×10^{-5}	8.3×10^{-6}	$(K \times 10^6)$ 1.433	$(K \times 10^6)$ 0.919
	 Aniline-*o*-sulphonic acid	 Aniline-*p*-sulphonic acid (Sulphanilic acid)	Heat and H_2SO_4	3.3×10^{-3}	5.81×10^{-4}	2.519	1.764
19	 Methyl aniline	 *o*-Toluidine	Heat	7.4×10^{-9}	1.09×10^{-9}	$(K_b^{60^\circ} + 10)$ 0.869	$(K_b^{60^\circ} \times 10^9)$ 0.038
	 Phenyl sulphamic acid	 Aniline-*o*-sulphonic acid	Heat and H_2SO_4	1.00×10^{-1}	3.3×10^{-3}	4.000	2.518
	$C_6H_5NH.NH_2$ Phenyl hydrazine	 *p*-Phenylene diamine	Heat and HCl	(K^{40°) 1.6×10^{-9}	(K^{25°) 3.1×10^{-10}	(Log. $K \times 10^{10}$) 1.204	(Log. $K \times 10^{10}$) 0.492

* See Section 5.

5. Rearrangements of Unsaturated Acids.

The most thorough test of the principle that true rearrangements of acids or bases of the non-reversible type take place in the direction to decrease the free energy of ionization is that given by the unsaturated acids. Rearrangements of such acids are so common that Thiele's partial valence theory was advanced for the explanation of the reason that $\Delta^{1},^{3}$ unsaturated acids gave Δ^2 unsaturated acids upon reduction. Further in the literature on unsaturated acids it is constantly noted that Δ^2 unsaturated acids rearrange to the Δ^1 isomer, etc.

Fichter and Pfister[1] first called attention to the fact that the Δ^2 unsaturated acids of the aliphatic series give a greater ionization constant than any of their isomers. The following figures and data will show this principle to be generally true in both open-chain and ring unsaturated acids. In the figures, the ordinates give the Briggsian logarithms of the affinity constants while the abscissas give the positions of the unsaturation in the acids, given in the table following the figures. The logarithm of the affinity constant is used rather than the algebraic value, since the free energy of ionization is proportional to a logarithmic function of the affinity constant and, also, since a comparison of the relative stabilities of the acids toward ionization is desired.

The principle of Fichter and Pfister appears to be general and not a single exception to it is known, while the data given in Table II show that it has been tested for twenty acids. In the case of Δ^1-tetrahydrophthalic acids an apparent exception to this rule is found, which disappears if we start the nomenclature with the other carboxyl so that the Δ^1 and Δ^2* positions are interchanged. The position of the double union then corresponds to that given in the other 18 acids. As Table I shows, these acids all rearrange in the direction to decrease the free energy of ionization so that it may be stated as a general rule *that whenever the unsaturation is Δ^2 with respect to a given carboxyl group true rearrangements of the non-reversible type are possible.*

Thiele and others have found that $\Delta^{1,3}$ unsaturated acids upon reduction give the Δ^2 acids, which, according to the above paragraph, are the most unstable toward ionization of any of their isomers, and rearrangements would be predicted and have been observed quite generally. Nernst states that such unstable isomers are formed under conditions where the speed of reaction at the time of formation is very slight. The above discussion of the reduction of the terephthalic acid showed that when precaution was taken to maintain conditions of slow speed of reaction and to use weak reducing agents the $\Delta^{2,5}$ unsaturated acid resulted.

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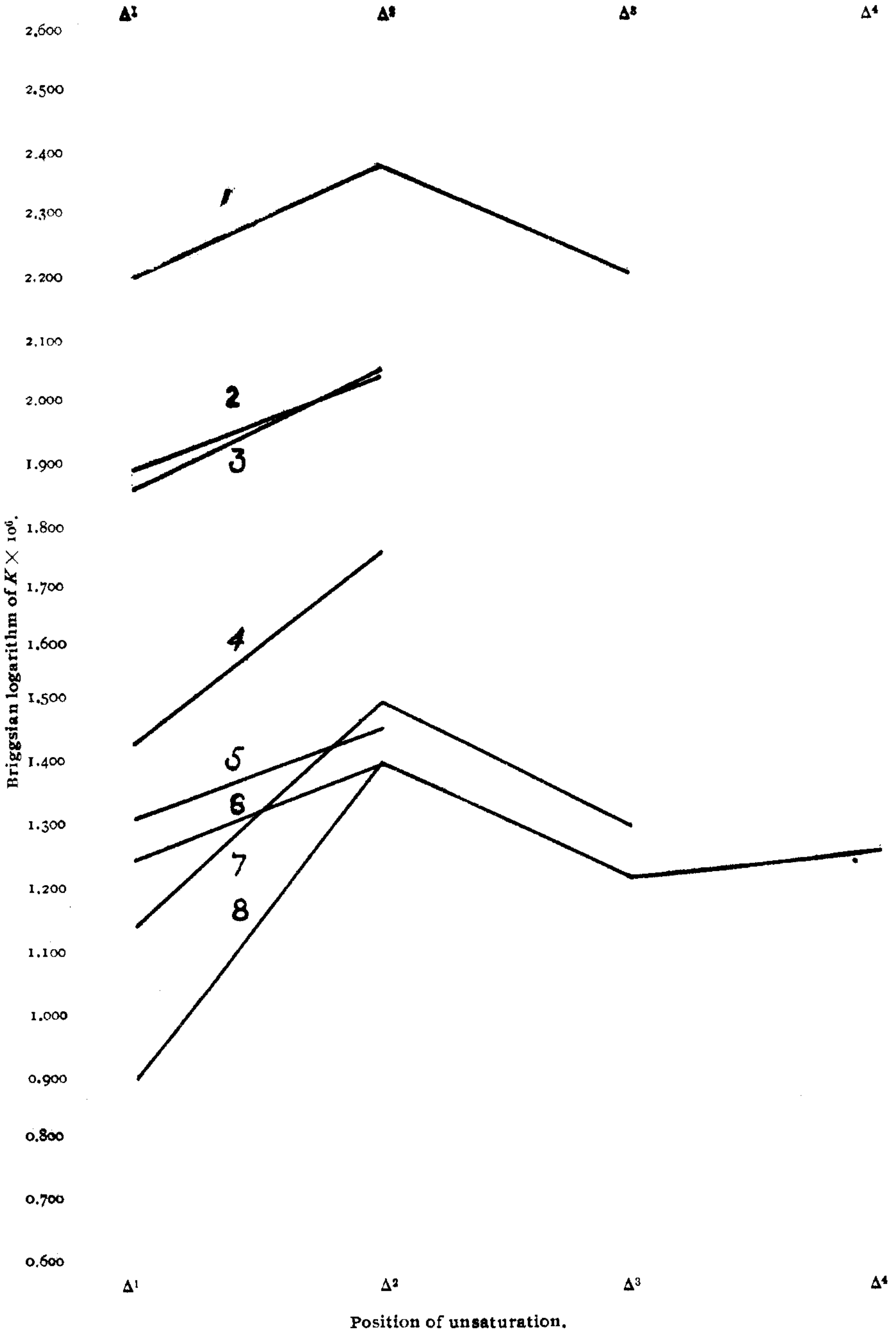
[1] Fichter and Pfister, *Ann.*, **334**, 203 (1904).

* See Tables I and II.


Δ1
Δ2
Δ3
Δ4
2,600
2,500
2,400
2,300
2,200
2,100
2,000
1,900
1,800
1,700
1,600
1,500
1,400
1,300
1,200
1,100
1,000
0,900
0,800
0,700
0,600
1
2
3
4
5
6
7
8
Briggsian logarithm of K × 10⁶.
Δ1
Δ2
Δ3
Δ4
Position of unsaturation.

This acid has both double unions Δ^2 to carboxyl groups. It should have the greatest amount of free energy of ionization according to the principle of Fichter and Pfister and should undergo rearrangements, which agrees with the experimental facts as shown above. *Hence it is evident that the compounds from which Thiele deduced his theory of partial valence, as well as other acids which obey the same rule, must be compounds which are formed with weak reducing agents involving small energy changes and where the speed of reaction is small so that compounds result which are very unstable toward ionization, and therefore toward rearrangement.*

TABLE II.—DATA FOR FIG. 1.

Curve number.	Name.	Ionization constant.	
		K.	Log. $K \times 10^6$.
1*	$\Delta^{2,6}$-Dihydrophthalic acid	1.65×10^{-4}	2.218
	$\Delta^{2,5}$-Dihydrophthalic acid	2.46×10^{-4}	2.392
	$\Delta^{2,4}$-Dihydrophthalic acid	1.5×10^{-4}	2.177
2	Δ^1-Dihydro-α-naphthylic acid	8.1×10^{-5}	1.909
	Δ^2-Dihydro-α-naphthylic acid	1.14×10^{-4}	2.058
3*	Δ^2-Tetrahydrophthalic acid	7.5×10^{-5}	1.876
	Δ^1-Tetrahydrophthalic acid	1.18×10^{-4}	2.0725
4	Δ^1-Dihydro-β-naphthylic acid	2.9×10^{-5}	1.463
	Δ^2-Dihydro-β-naphthylic acid	5.1×10^{-5}	1.772
5	Δ^1-Tetrahydrobenzoic acid	2.21×10^{-5}	1.345
	Δ^2-Tetrahydrobenzoic acid	3.05×10^{-5}	1.485
6	Δ^1-Hexenoic acid	1.89×10^{-5}	1.277
	Δ^2-Hexenoic acid	2.64×10^{-5}	1.428—
	Δ^3-Hexenoic acid	1.74×10^{-5}	1.241
	Δ^4-Hexenoic acid	1.91×10^{-5}	1.282
7	Δ^1-Pentenoic acid	1.48×10^{-5}	1.172
	Δ^2-Pentenoic acid	3.35×10^{-5}	1.526
	Δ^3-Pentenoic acid	2.09×10^{-5}	1.322
8	Δ^1-Cycloheptene carboxylic acid	8.3×10^{-6}	0.919
	Δ^2-Cycloheptene carboxylic acid	2.7×10^{-5}	1.432

6. Illustrations of True Rearrangements of Non-reversible Type.

The following table is a list of some of the more important true rearrangements of the non-reversible type. Many other illustrations of the rearrangements of Δ^2 unsaturated acids to their Δ^1 isomers are known for which no measurements of the ionization constants have been made. Yet in the light of the above discussion it is safe to conclude that they take place in the direction to decrease the free energy of ionization.

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* See Section 5.

TABLE III.

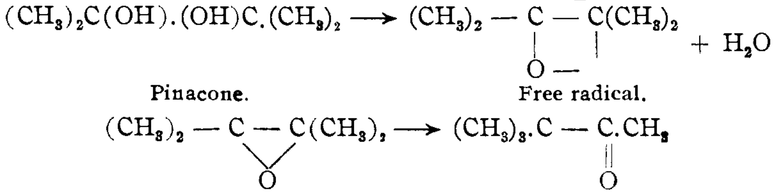
Class.	True rearrangements (non-reversible type).		Catalyzer.
	Before.	After.	
I	Dihydrosorbic acid	Δ^{1}-Hexenoic acid	OH^-
	Eugenol	Isoeugenol	OH^-
2	Δ^{2}-Tetrahydrobenzoic acid	Δ^{1}-Tetrahydrobenzoic acid	OH^-
	$\Delta^{3,5}$-Dihydrophthalic acid	$\Delta^{2,6}$-Dihydrophthalic acid	OH^-
	* Δ^{1}-Tetrahydrophthalic acid	Δ^{2}-Tetrahydrophthalic acid	OH^-
	Δ^{2}-Tetrahydroterephthalic acid	Δ^{1}-Tetrahydroterephthalic acid	OH^-
	$\Delta^{2,5}$-Dihydroterephthalic acid	$\Delta^{1,5}$-Dihydroterephthalic acid	OH^-
	$\Delta^{1,5}$-Dihydroterephthalic acid	$\Delta^{1,4}$-Dihydroterephthalic acid	OH^-
	$\Delta^{2,6}$-Dihydroterephthalic acid	$\Delta^{1,4}$-Dihydroterephthalic acid	OH^-
	$\Delta^{1,3}$-Dihydroterephthalic acid	$\Delta^{1,4}$-Dihydroterephthalic acid	OH^-
	Aniline-*o*-sulphonic acid	Aniline-*p*-sulphonic acid	H_2SO_4 and heat
9	Acetohydroxycrotonic ester	Diacetoacetic ester	$NaOOC.CH_3$ and acetic anhydride
	Isoacetophenone ethyl ether	Phenylpropylketone	Boiling under pressure
13	Phenylmethylketoxine	Acetanilide	Acids
	(Beckmann's rearrangement)		Acid chlorides and anhydrides
14	Benzaldoxime-benzylether	Benzylbenzamid	Acid chlorides
	Methylaniline	*o*-Toluidine	Heat
	Alkyl iodides of aniline	Alkylated aniline hydroiodides	Heat
	Benzidine	Rearrangements	H^+
	Semidine	Rearrangements	H^+

17	Alkyl isocyanides	Alkyl cyanides	Heat
18	Phenylpyrazole methyliodide	Phenylmethylpyrazole hydroiodide	Heat
	Alkyl pyridinium iodides	Alkyl pyridines	Heat
19	Diacetanilide	*p*-Acetoacetanilide	$ZnCl_2$
	p-Amino acetophenol	*p*-Hydroxyacetanilide	OH
	Diazamino compounds	Aminoazo compounds	Hydrochloride of amine
	Benzidine	Rearrangements	H+
	Semidine	Rearrangements	H+
	Methylaniline	*o*-Toluidine	Heat
	Nitrosamine of methylaniline	*p*-Nitrosomethylaniline	Heat
	Phenyl nitramine	*o*- and *p*-Nitraniline	Heat
	Phenyl sulphamic acid	Aniline-*o*-sulphonic acid	Acetic acid + H_2SO_4
	Diacyl anilide	*p*-Aceto-acetanilide	$ZnCl_2$
	Acyl haloanilides	*p*-Halo-acetanilides	Glacial CH_3COOH
	Phenyl hydroxylamine	*p*-Hydroxyaniline	Mineral acids
	Phenyl hydrazine	*p*-Phenylenediamine	Strong acids and heat
	Beckmann's rearrangements		Acids, acid chlorides, acid anhydrides
25	Benzoyl-*p*-hydroxyaniline	*p*-Hydroxybenzoylanilide	OH–
	Acetyl *p*-hydroxyaniline	*p*-Hydroxyacetanilide	OH–
	Aminophenylcarbonate	Phenolurethane	Heat
	Iminoether of formanilide	Ethyl formanilide	Heat
	Benzimido ethyl ether	Ethyl benzamide	Heat
	Cyanuric esters	Isocyanuric esters	Heat

* See Section 5.

7. Rearrangements with Reaction.

In Table IV a few examples of molecular rearrangements with reaction are given. The numbers in the first column of the table refer to the classes of Table V. With rearrangements of this type, it is much more difficult to distinguish any regular behavior. If such rearrangements are grouped according to the kind of reaction by which they are formed, some uniformity is obtained. Thus rearrangements taking place simultaneously with dehydration appear to be due to the fact that a free radical cannot exist for a measurable time or that a possible intermediate ring compound is too unstable toward rearrangement to exist. This is illustrated by the pinacone-pinacolin change:



Pinacone. Free radical.

Unstable ring compound. Pinacolin.

In the case of the reduction of the unsaturated acids, the speed of the reaction and the strength of the reducing agent control the rearrangement. For example, if $\Delta^{1,3}$-dihydrobenzoic acid is reduced in the cold by sodium amalgam, the Δ^2-tetrahydro acid results, and there has been a shifting of the double union either from the Δ^1 or Δ^3 position to the Δ^2 position. If this same reaction is performed with the same reagents at a higher temperature the Δ^1-tetrahydrobenzoic acid results and there has been no shifting of either double union. A review of Fig. 1 and Tables I and II shows that the acid having two double unions within the molecule possesses more free energy of ionization than any of its dihydro reduction products. Further, the figure shows that the Δ^2 unsaturated acid has the greatest amount of free energy of ionization of any of its isomers. Hence, when Δ^2-tetrahydrobenzoic acid was formed by the reduction of $\Delta^{1,3}$-dihydrobenzoic acid, the decrease in the free energy of ionization was a minimum and a double union was shifted. With the same reagents, at a higher temperature, *i. e.*, where the speed of reaction was greater, reduction of the $\Delta^{1,3}$-dihydrobenzoic acid gave the Δ^1-tetrahydrobenzoic acid. The data for Fig. 1 show that the difference in the free energy of ionization of the $\Delta^{1,3}$ acid and its Δ^1-dihydro reduction product is much greater than in the case above where the Δ^2-dihydro reduction product was formed. Further, the formula for these acids show that there has been no shifting of the double union in the latter reduction. Therefore, *when the reduction of unsaturated acids containing more than one double union takes place so that the decrease in the free energy of ionization is a minimum, compounds form simultaneously*

TABLE IV.

	Rearrangements with reaction.		
Class.	Before.	After.	Reaction.
1	Pinacone	Pinacolin	Dehydration
	3,3-Dimethyl butanol	Tetramethyl ethylene	Dehydration
	α,α-Dimethylglutaconic acid, 2	α,α'-Dimethylglutaric acid	Reduction
	Tetraphenylethylene	Benzoyl triphenyl methane	Oxidation
	Hydrobenzoin	Diphenylacetaldehyde	Dehydration
	Benzil	Benzilic acid	Hydration
	$\Delta^{1,3}$-Unsaturated acids (Open chain)	Δ^{2}-Unsaturated acids (Open chain)	Reduction
2	Triphenylmethane color bases	Triphenylmethane dyes	Dehydration
	Phenyl dimethyl indolinol	Dimethyl indole	Dehydration
	Gem-dimethyldihydroresorcinol	Dichloro-*o*-xylene	Chlorination
	$\Delta^{1,3}$-Dihydroterephthalic acid	Δ^{2}-Tetrahydroterephthalic acid	Reduction
	$\Delta^{1,4}$-Dihydroterephthalic acid	Δ^{2}-Tetrahydroterephthalic acid	Reduction of brominated acid
	$\Delta^{2,5}$-Dihydroterephthalic acid	Δ^{2}-Tetrahydroterephthalic acid	Reduction in cold
	Terephthalic acid	$\Delta^{2,5}$-Dihydroterephthalic acid	Reduction in cold
	α,α'-Dibromhexahydroterephthalic acid	$\Delta^{1,3}$-Dihydroterephthalic acid	Dehalogenation
	Phthalic acid	Δ^{2}-Tetrahydrophthalic acid*	Reduction + heat
	Benzoic acid	Δ^{2}-Tetrahydrobenzoic acid	Reduction
	$\Delta^{1,3}$-Dihydrobenzoic acid	Δ^{2}-Tetrahydrobenzoic acid	Reduction in cold
	$\Delta^{1,3}$-Dihydrobenzoic acid	Δ^{1}-Tetrahydrobenzoic acid	Reduction + heat
3	Triphenylmethane dyes	Tiyphenylmethane color bases	Hydration
	Isogeraniolene	*v*-Trimethylbenzene	Bromination and dehydration
	Isogeraniolene	Pseudocumene	Bromination and dehydration

* See Section 5.

with a rearrangement and these compounds, in turn, will undergo rearrangement.

This class of rearrangements furnishes many fine illustrations of Ostwald's *law of successive reactions.*[1]

8. Review of the Field of Molecular Rearrangements.

The conclusions, given in the preceding paragraphs, are based on a general review of the field of molecular rearrangements. In this review, the need of a classification of the mass of material included under the term molecular rearrangement has been very evident. Not only should such reactions be classified as reversible and non-reversible rearrangements of the types discussed above, but the behavior of the different radicals should be thoroughly studied.

Classes of Known Rearrangements.

Table V has been developed to show the present state of the problem of rearrangement. In the first vertical column a partial list of the elements and radicals has been given. In the first horizontal row is given the elements between which the rearrangement occurs, while the second horizontal row gives their position in the compound, that is, whether in the ring or side chain. The third horizontal row gives the class to which each rearrangement of a given group is assigned. In the first horizontal row the letter stands for the atomic symbol of the element and the arrow shows the direction of the rearrangement. In the second row Op stands for open chain, R for closed chain or ring, Op $\longrightarrow$ R for open or side chain to closed chain, and R $\longrightarrow$ Op from closed to open or side chain. Thus to read the behavior of the alkyl group for class I, it is evident that the alkyl group will rearrange from carbon to carbon in the open chain; or for class 8, it is evident that the alkyl group may rearrange from carbon in the ring to oxygen in the side chain. Those rearrangements which are theoretically impossible because of the law of constant valence are designated by the sign x, while those impossible for the trivalent but possible for the pentavalent nitrogen are designated by the sign v.

To show the present state of knowledge of the phenomenon of rearrangements, the following system of marking is employed in the vertical columns beneath the classes:

o designates occasional occurrence,
c designates common occurrence, and
r designates rare occurrence.

Doubtless the above scheme is incomplete so far as the known cases are concerned, but it must be borne in mind that such a table when completed will demand many years of careful reading, especially in a field where systemization has not been attempted.

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[1] Ostwald's *Lehrbuch*, II, 2, 445.

TABLE V.

Element or radical.	C → C				C → O				O → C				C → N				N → C				O → O				O → N				N → O				N → N			
	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op
Class.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
Alkyl	o	o		o		x	x		o	x		x					c	c	c			x	x	x	c	x		x		x	x					
Aryl	c					x	x			x		x	c									x	x	x		x		x		x	x					
Acyl						x	x		o	x		x							c			x	x	x	o	x		x		x	x					
Aracyl						x	x		o	x		x										x	x	x	o	x		x		x	x					
Hydroxyl						x	x			x		x							c			x	x	x		x		x		x	x					
Oxyalkyl						x	x			x		x										x	x	x		x		x		x	x					
Oxyaryl						x	x			x		x										x	x	x		x		x		x	x					
Aldehyde						x	x			x		x										x	x	x		x		x		x	x					
Carbonyl						x	x			x		x										x	x	x		x		x		x	x					
Carboxyl						x	x			x		x										x	x	x		x		x		x	x					
Carboxyalkyl						x	x			x		x										x	x	x	r	x		x		x	x					
Carboxyaryl						x	x			x		x										x	x	x		x		x		x	x					
Amine						x	x			x		x							c			x	x	x		x		x		x	x					
Alkylamine						x	x			x		x										x	x	x		x		x		x	x					
Arylamine						x	x			x		x							c			x	x	x		x		x		x	x					
Nitro						x	x			x		x							o			x	x	x		x		x		x	x					
Nitroso						x	x			x		x							o			x	x	x		x		x		x	x					
Isonitroso					x	x	x	x	x	x	x	x		v	v			v		v	x	x	x	x	x	x	x	x	x	x	x	x		v	v	v
Hydrogen	c	c		c	c	x	x	c	c	x	o	x	c	c		c	c		c		c	x	x	x	c	x	x	x		x	x					
Halogen						x	x			x		x							c			x	x	x		x		x		x	x					
Sulphonic						x	x			x		x							c			x	x	x		x		x		x	x					
Double union	c	c	c	c	c	x	x	c	c	x	c	x	c	c		c	c		c			x	x	x	c	x		x	c	x	x					

TABLE VI.—ILLUSTRATION OF THE DIFFERENT CLASSES OF MOLECULAR REARRANGEMENTS GIVEN IN TABLE V.

Class.	Radical or element.	Rearrangement.	
		Before.	After.
1	Alkyl	Pinacone	Pinacolin
	Aryl	Tetraphenyl ethylene	Benzoyltriphenylmethane
	Hydrogen	Dihydrosorbic acid	Δ^1-Hexenoic acid
	Double union	Dihydrosorbic acid	Δ^1-Hexenoic acid
2	Alkyl	*gem*-Dimethyldihydroresorcinol	Dichloro-*o*-xylene
	Hydrogen	Δ^2-Tetrahydrobenzoic acid	Δ^1-Tetrahydrobenzoic acid
	Double union	Δ^3-Tetrahydrobenzoic acid	Δ^1-Tetrahydrobenzoic acid
	Sulphonic	Aniline-*o*-sulphonic acid	Aniline-*p*-sulphonic acid
3	Double union	Fuchsine	Rosaniline
4	Double union	Rosaniline	Fuchsine
5	Hydrogen	Enol-acetoacetic ester	Keto-acetoacetic ester
8	Hydrogen	Keto-phloroglucinol	Enol-phloroglucinol
	Double union	Enol-phloroglucinol	Keto-phloroglucinol
9	Alkyl	Isoacetophenone ethyl ether	Phenylpropylketone
	Acetyl	Acetohydroxycrotonic ester	Diacetoacetic ester
	Benzoyl	Acetophenone-*o*-benzoate	Dibenzoylmethane
	Hydrogen	Keto-acetoacetic ester	Enol-acetoacetic ester
	Double union	Keto-acetoacetic ester	Enol-acetoacetic ester
11	Hydrogen	Enol-phloroglucinol	Keto-phloroglucinol
	Double union	Keto-phloroglucinol	Enol-phloroglucinol
13	Aryl	Phenylmethyl ketoxime	Acetanilide
	Hydrogen	Tautomerism—Amide	Imide type
	Double union	Tautomerism—Amide	Imidol type
14	Hydrogen	Phenylpyrazolone methyl iodide	Phenylmethylpyrazole
16	Hydrogen	Methylaniline	*o*-Toluidine
	Double union	Rosaniline	Fuchsine
17	Alkyl	Alkyl isocyanides	Alkyl cyanides
	Aryl	Phenyl isocyanide	Benzonitrile
	Hydrogen	Tautomerism—Imide	Cyanide type
18	Alkyl	Phenylpyrazole methyl iodide	Phenyl methyl pyrazole
19	Alkyl	Methylaniline	*o*- and *p*-Toluidines
	Acyl	Diacetanilide	*p*-Acetylacetanilide
	Hydroxyl	Phenylhydroxylamine	*p*-Aminophenol
	Amine	Phenyl hydrazine	*p*-Phenylenediamine
	Arylamine	Hydrazobenzene	Benzidine
	Nitro	Phenyl-nitramine	*o*- and *p*-Nitraniline
	Nitroso	Nitrosamine of methylaniline	*p*-Nitrosomethylaniline
	Hydrogen	Tautomerism—Azo	Hydrazo type
	Halogen	Acylchloranilides	*p*-Chloroacetanilides
	Sulphonic	Sulphamic acid	Aniline-*o*-sulphonic acid
	Double union	Fuchsine	Rosaniline
21	Hydrogen	*p*-Nitrophenol	*p*-Isonitrophenol
25	Alkyl	Imino ether of formanilide	Ethyl formanilide
	Acyl	*p*-Aminoacetophenol	*p*-Hydroxyacetanilide
	Benzoyl	*p*-Amino-benzoylphenol	*p*-Hydroxybenzanilide
	Carboxyalkyl	Amino-phenylcarbonate	Phenol urethane
	Hydrogen	Tautomerism—Amide	Imidol type
29	Hydrogen	Tautomerism—Amide	Imidol type

This table, in conjunction with Tables III and IV, shows that hydrogen, the double union (which in general is the same thing as the shifting of hydrogen) and the alkyl group are more generally rearranged than the other elements or radicals. Further, rearrangements occur much more frequently between nitrogen and carbon, the shifting occurring from side-chain nitrogen to ring carbon. The alkyl, acyl, aromatic acid radical, hydroxyl, amine, alkylamine, arylamine, nitroso, nitro, halogen and sulphonic radicals undergo this rearrangement (members of class 19). In general, however, the oxyalkyl, oxyaryl, and alkyl, aryl, nitro, nitroso, and haloamine groups do not rearrange as a whole, but rather the alkyl, aryl, nitro, nitroso and halogens shift from the oxygen or nitrogen to carbon.

The classes given in the tables, refer to this scheme of classification, and Table VI gives illustrations of rearrangements of different elements and radicals belonging to these classes.

Summary.

1. Molecular rearrangements of carbon compounds are of the reversible and non-reversible types of chemical reactions.

2. Molecular rearrangements of carbon compounds must be further classified according as the rearrangement is simply a readjustment of the atoms already present in the molecule (true rearrangements) or as the rearrangement is due to atoms having been added to or taken away from the original molecules (rearrangements with reaction).

3. Compounds which rearrange are formed under conditions where the speed of formation is a minimum so as to produce substances very unstable toward arrangements.

4. The reagents present when a compound undergoes true rearrangement of the non-reversible type are catalytic to the speed of the rearrangement.

5. True rearrangements of the non-reversible type take place in the direction to produce substances more stable toward rearrangement.

6. True rearrangements of acids and bases belonging to the non-reversible type take place in the direction to produce acids and bases more stable toward ionization (*i. e.*, having less free energy of ionization) and therefore the logarithm of the ionization constant may be used as a criterion of stability in these rearrangements.

7. An organic acid, which possesses a double union Δ^2 to its carboxyl group, has a greater free energy of ionization than any of its isomers and may, therefore, readily undergo rearrangements to produce isomers more stable toward ionization and rearrangement.

8. Δ^2 Unsaturated acids are formed from $\Delta^{1,3}$ unsaturated acids under the conditions where the speed of formation is a minimum, the de-

crease in the free energy of ionization is a minimum, and the stability toward rearrangement is a minimum.

9. Many rearrangements with reaction are due to the fact that a free radical cannot exist, and after certain atoms or groups have been eliminated the very unstable radical resulting undergoes a readjustment of the atoms present so as to maintain the quadrivalent nature of carbon and produce a substance more stable toward rearrangement.

10. A schematic review of the field of molecular rearrangements of carbon compounds is given by Table V, and Table VI gives illustrations of the classes of rearrangements designated in Table V.

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THE INVERSION OF CANE SUGAR BY INVERTASE. VII. THE EFFECT OF ALCOHOL ON INVERTASE.

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Purpose of the Investigation.

A knowledge of the action of alcohol on invertase is of practical importance for two reasons: first, alcohol is naturally present during the fermentation of cane sugar by yeast and the invertase of the yeast is thus normally in the presence of weak alcohol; and, second, alcohol is often used, though generally with little success, to prepare the enzyme in a solid form by precipitation from an aqueous extract of yeast. In order to learn what influence alcohol of different strengths has on invertase, the following investigation was made. The results show that the influence is exceedingly great and that it consists in three distinct actions, namely, an inactivation, a permanent destruction, and a precipitation of the enzyme. These actions will be described in the order named.

The Inactivation of Invertase by Alcohol.—The activity of purified invertase in inverting cane sugar dissolved in various strengths of ethyl alcohol was measured at 30° by the usual method. Care was taken to have sufficient acetic acid in the solutions to insure that the maximum activity of the enzyme was attained, and the solutions were made alkaline at the end of the experiment to stop the enzymatic action and complete the mutarotation. The alcohol used was Squibb's or Baker's absolute alcohol and the concentrations are expressed as volume per cent. The activities are recorded in Table I as the velocity coefficients of the inversion, using minutes and decimal lagarithms and multiplying by