

contain sufficient potassium to cause the precipitation of acid tartrate when large amounts of tartaric acid are involved in an analysis. Working with purified acids, the curves were constructed for amounts of tartaric acid up to 1.0 g.; they are published through 0.8 g. only, however, since that is the limit of use in practice.

The qualitative composition of a material to be analyzed should be known since results are sometimes open to question when the point of intersection on the graph falls close to one side. As an example of this, it will be noticed that in Nos. 705 and 706, the data indicate an apparently negative amount of tartaric acid, whereas Nos. 709 and 710, from the same batch of juice, show tartaric to be present.

Although the method is not yet everything that could be desired, nevertheless it is believed that it does constitute an easy and fairly reliable means of assaying these two acids when occurring singly or together.

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THE CONFIGURATIONS OF ORGANIC COMPOUNDS AND THEIR RELATION TO CHEMICAL AND PHYSICAL PROPERTIES.

BY ARTHUR MICHAEL.

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The experimental proof¹ that in the addition of halhydric acids and halogens to acids of the acetylene series, and in the reverse elimination reactions, trans-processes are favored, showed that the then adopted configurations of all stereomeric substances, excepting those given by van't Hoff to the dibasic, unsaturated acids, had to be reversed, as they had been based on the Wislicenus hypothesis of the occurrence of cis-processes.² In the new classification a more marked connection between the energy-content and many of the physical properties could be traced, although certain groups of stereomers showed anomalous properties.³ Since then, there has been very little progress made in this direction; indeed, recently, Pfeiffer⁴ stated that *a priori*: "It is hardly possible to decide from the configuration which of the stereomers has the higher melting point, or represents the more stable modification."

It will be shown that it is possible to coördinate these relations and to explain the apparent exceptions, but it should be emphasized that van't

¹ Michael, *J. prakt. Chem.*, [2] 52, 289 (1895).

² *Ibid.*, 359-365. The configurations given by Pfeiffer (*Z. physik. Chem.*, 48, 55-62 (1904)), which were based on my experimental results, were not new, as is sometimes stated in text books and papers, but were a repetition of those given in my paper (*Ibid.*, 363).

³ Michael, *Ibid.*, 345; *Ber.*, 34, 3644, footnote 4 (1901).

⁴ *Z. physik. Chem.*, 48, 57 (1904).

Hoff's first theorem, which presupposes a radical difference in the spacial relations of the axial carbons and in the nature of their rotation, in saturated and unsaturated substances, has been not only experimentally disproven,¹ but all the reasons advanced in its favor are untenable.² This conclusion follows, too, from the second law of thermodynamics, since in every organic molecule a rotation about a common carbon axis must take place if thereby an increase of entropy will result, and its free energy is able to overcome the hindrance to the change. The extent of this hindrance, which represents the stability of the stereomer, is, primarily, the bound energy of the carbon atoms at the axis, and that existing spacially between the atoms directly or indirectly joined to them. After this entropic status has been established, no further rotation is possible as long as the energy conditions remain unchanged. This condition does not imply, however, that the atoms are then static; indeed, it is absolutely necessary to assume that they are all in a more or less condition of vigorous oscillation, although in a restricted sphere.³

The ability of unsaturated stereomers and the corresponding saturated substances to rotate is simply one of degree.¹ In the latter group the advent of a relatively slight physical or chemical force may cause such a change, and it is due to this slight hindrance that, excepting comparatively restricted groups of bodies, saturated derivatives exist in only one modification.

According to Wunderlich⁴ a carbon atom may be a homogenous sphere with four equal segments, where chemical union with other atoms takes place. A simpler hypothesis, and the most probable spacial conception, is to accept, with Werner,⁵ a sphere as the form and connect it with the view of the writer,⁶ that, in removing an atom from each of two adjacent radicals in an organic, saturated substance, part of the energy thus liberated appears as free chemical energy at the unsaturated carbons, and part goes to increase the bound energy between these carbons and, spacially, between all the atoms joined to them; and, also, with the view of Richards⁷ that atoms are compressible by chemical force.

The energy and the affinity relations of a carbon, which is joined to three atoms or groups, evidently depend on their chemical nature; if the relations are such that it may unite with the unsaturated carbon in a

¹ Michael, *J. prakt. Chem.*, [2] 46, 425 (1892).

² Michael, *Ann.*, 390, 39 (1912).

³ Otherwise, it is not possible to explain the fact that atoms may stand in practically the same spacial relation to two or more other atoms in the molecule.

⁴ "Konfiguration organischer Moleküle," 1886, see, also, Auwers, "Entw. der Stereochemie," 1890, pp. 18-35.

⁵ *Lehrb. d. Stereochemie*, pp. 15, 186 (1904).

⁶ *J. prakt. Chem.*, [2] 60, 298 (1899).

⁷ THIS JOURNAL, 36, 2417 (1914).

similar radical,¹ then part of the free energy in these carbons will be changed into bound energy and heat, and the same energy transformation will take place spacially between the atoms or groups joined to them. In this conversion of free into bound energy these carbon spheres are compressed together to form a segment, the size of which depends on the magnitude of the energy changes that occur between the carbons and spacially between the atoms of the groups joined to them. This segmentation of the axial carbons should be less in *cis*- than in *trans*-succinic acid for two reasons: First, the negative energy of the carboxyls is less neutralized by the nuclear hydrogens; in consequence, the axial carbons are relatively more negative and have, therefore, less affinity for each other. Secondly, the smaller conversion, spacially, of the free energy in the atoms joined to the axial carbons.

Since unsaturation is accompanied by an increase in the bound energy at the axial carbons, the extent of their segmentation, must be greater in unsaturated than in the corresponding saturated stereomers; while the free energy of the axial carbons must be greater in the maleinoid than in the fumaroid form, the extent of the segmentation must be smaller. In the act of unsaturation, therefore, not only do the masses of the axial carbons become condensed, but the spacial distance becomes less between all atoms in *cis*-positions joined to them.

Further, the energy necessary to cause a rotation of atoms or groups about the axial carbons must be far less in saturated than in the corresponding unsaturated derivatives, and in the latter bodies less for the maleinoid than for the fumaroid forms.

The principal points of accumulation of the free energy in stereomeric, unsaturated acids, are at the unsaturated carbons, carbonyl and hydroxyl groups; and its extent, as manifest in their atoms, depends on their direct and spacial relations to the other atoms in the molecules. Evidently, the relative values of the sum total of the free energy in all the atoms of such stereomers are in a direct relation to those of their heats of combustion, and, as Stohmann² has shown that these factors and the affinity constants of simple stereomeric derivatives of acrylic acid are in a direct relationship, the latter values in such acids must stand in a direct proportion to the total free energy.³ This connection justifies classifying these stereomeric acids as maleinoid or fumaroid on the basis of the magnitude of their affinity constants.

The classification refers, however, only to the proportion of the total free energy in the stereomers, and it does not necessarily follow that the

¹ THIS JOURNAL, 32, 996 (1910).

² *J. prakt. Chem.*, [2] 40, 357 (1889); 46, 530 (1892).

³ Michael, *Amer. Chem. J.*, 39, 2 (1908); Michael and Bunge, *Ber.*, 41, 2907 (1908).

relations, as shown at the acidic hydrogens, represent, also, the relative values of all the other atoms in the molecules.

Acetylenic linkage, as a further development of double, brings the carbon spheres in contact over a larger segment than in the corresponding ethylenic configuration, and causes an augmentation of the free energy at the axial carbons, with a further spacial juxtaposition of the atomic groups. In this class only one, the cis-derivative, exists, owing to the great difference between it and a trans-form in the energy of the two systems.¹

Butyric acid may exist in the stereostructures:²



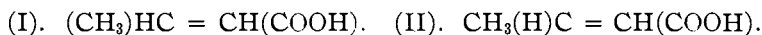
Owing to the slight hindrance to rotation in saturated, monobasic acids the free acid should have the stereoform representing the maximum intramolecular, atomic neutralization, and, therefore, the smaller affinity constant. With a base, the system should endeavor to realize the maximum increase of entropy, and the acid should assume the more acidic configuration, provided the difference between the heats of neutralization of the two forms by the base is sufficient to overcome the slight hindrance to rotation. Essentially the same relation arises in the behavior of butyric acid toward the relatively basic water, and the affinity constant of the acid represents, therefore, the value of the more acidic stereo-

¹ The free energy in CH_2 , when introduced in a fatty hydrocarbon without change in saturation, is largely transformed into bound energy and heat, and the latter is dissipated. On the other hand, when two such radicals unite, a much larger proportion of their free energy remains unchanged and, as less heat is lost, the thermic value of CH_2 must be greater in ethylene than in a saturated hydrocarbon. Acetylene, often miscalled a "spontaneously decomposable" substance, is unstable only in the sense of reactivity, due to the great free energy in the system. Its formation at a high temperature from so many organic bodies, conforms with the general tendency under such conditions to form systems with greater content of free energy; it is then stable to a high temperature (*c.* 1300°), when the heat-energy overcomes the bound energy between the carbons and hydrogens, and it passes over into the towards heat more stable system of hydrogen and a highly polymerized carbon. Misleading, too, is its classification as an endothermic body; it is so only in reference to a very complex form of carbon, which would be formed from a diatomic modification with a tremendous conversion of free into bound energy and heat. Strictly speaking, endothermic and exothermic should only be used when the thermic values are obtained from reactions where the molecular conditions before and after the chemical change are comparable, or, when allowance may be made for differences. A revision of thermochemical data from this point of view would be of great help in disentangling the present confusion.

² This word, and stereoform, are suggested as synonyms for configuration. To represent spacial formulas, whenever it is possible, in a single line, atoms or groups in cis-position will be inclosed in parentheses, and the axial carbons denoted by a hyphen or hyphens. In some cases, it may be desirable to use asterisks, instead of parentheses, to indicate the cis-relation; and, with saturated compounds, to use the two methods simultaneously.

structure, while a solution of the acid in greater concentration may contain a mixture of the two configurations.

Bruni¹ has shown that organic substances with similar configurations form isomorphous mixtures, and that free butyric acid stands in this relation to crotonic acid; that is, it is the *fum. form.*² The anomalous rise of the affinity constants in passing from propionic (1.34)³ to butyric acid (1.5), has been explained⁴ by the negative C of the introduced CH₃ being spatially much nearer to H than the H₃. In *trans*-CH₃ the spacial relations of the elements are reversed, and, in consequence, the replacement of *trans*-H by CH₃ invariably lowers the affinity constant, which for *trans*-butyric acid, if it could exist in dilute aqueous solution, would be less than that of propionic acid, probably about 1.2. Owing to the much greater hindrance to rotation in unsaturated compounds, crotonic acid exists free in two forms:



These configurations may be derived from that of acrylic acid (5.6) by *cis*- or *trans*-replacement of H by CH₃, and the effect on the affinity constant must be to increase or to lower the value. The constant of crotonic acid (2) shows that it has the fumaroid configuration (II), which agrees, as will be shown, with all the physical and chemical properties of the acid.

It is generally accepted that the replacement of an atom or a group in a stereomeric substance does not lead to a relative change in the order of the configuration. As this conclusion follows directly from the present mechanical stereochemical theory, and as it has been a fruitful source of confusion, it is of importance to show that it is erroneous.

For this purpose, we shall consider the configurations of the chloro-crotonic acids in relation to their affinity constants and their properties.

¹ *Gazz. chim. ital.*, [2] 34, 495 (1905).

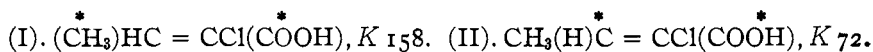
² Probably, at ordinary temperature, the free acid represents a dynamic mixture of many *fum.* and few *mal.* configurations, and the proportion of the latter should increase with heat increment; at the boiling point the relative relations may be reversed.

³ All of the affinity constants in this paper should be multiplied by 10⁻⁶ to obtain the absolute values.

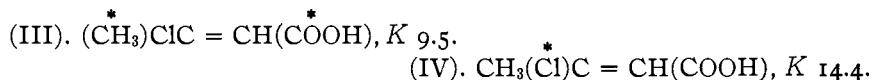
⁴ Michael, *J. prakt. Chem.*, [2] 60, 335 (1899). The "Scale of Combined Influence" —2, 3, 5, 6, 4, 7 (9, 10, 11), 8—*Ibid.*, 331; *THIS JOURNAL*, 32, 999 (1910); 34, 849 (1912) was first derived from the affinity constants of saturated, monobasic acids and applies,

therefore, only to atoms in *cis*-positions. H always signifies the acidic hydrogen in this paper.

α -Acids:



β -Acids:



Configuration (I) is derived from that of allocrotonic acid (6-7)¹ and (II) from that of crotonic acid (2). The effect of chlorine in the fifth position to the acidic hydrogen is clearly shown by the enormous increase in the values of the constants. And the much greater value of (I) is due, primarily, that in it the halogen is in the unimportant fourth place to the positive β -H, while in (II) it is in the very important fifth position to three such atoms; and, secondarily, that it is a derivative of allocrotonic acid. In agreement with the affinity constants and the energy relations, is the conversion of α -chloroallocrotonic (I) into α -chlorocrotonic acid (II) by heat or by mineral acids, and all the other physical properties of these compounds.

In the α -halogen crotonic acids the usual relations between the affinity constants and physical properties prevail, but in the β -acids they are largely reversed; for instance, the higher melting acid (94°) is more soluble and has the larger constant (14.4). Notwithstanding, it yields crotonic acid on reduction and goes over on heating into the lower melting form (60°). The derivative represented by configuration (III) is derived from that of allocrotonic acid, which is a factor in favor of a larger affinity constant, but in it the halogen is in the trans-position to H, and in the cis-position to α -H, while in IV it is in the cis- to H and in the trans-place to α -H. The negative energy of the Cl in (III) is, therefore, not only used up more than in (IV), but it influences the acidic hydrogen to a much less extent, and, since Cl has a much greater negative influence than CH₃,

¹ Ostwald's value is 3.6, but he used a preparation containing at least 50% of crotonic acid. Michael, *J. prakt. Chem.*, [2] 46, 236 (1892). It is very desirable that the term "allo" be restricted to its original use (Michael, *Ber.*, 19, 1384 (1886)), which is to denote the stereomer with the larger energy-content, *i. e.*, the maleinoid form. In this sense, it is far preferable to the term "iso," which is also used to represent structural isomerism. The name of the maleinoid modification may be always formed by prefixing "allo" to that of the fumaroid stereomer, and the energy relations of the compounds are shown with certainty in this way. To express the fact that some fumaroid derivatives form maleinoid addition products, "allo-" has been prefixed to the addendum (Michael, *Ber.*, 34, 3645 (1901)); thus, cinnamic acid and chlorine in the dark give cinnamic allo-dichloride. Absolutely wrong, is the use of α - and β - to indicate stereoisomerism, when there is a possibility of confusion with the accepted structural use. It is unfortunate, that the suggestion (*Ibid.*, 19, 1381) to use some contraction for allo has not been adopted.

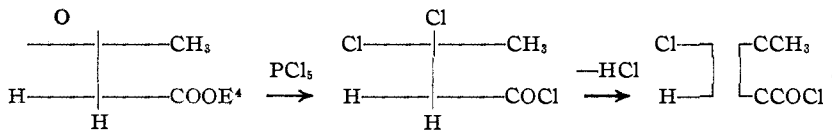
the last two factors outbalance the comparatively slight difference between the affinity constants of the mother acids, and cause the reversion in the relations of the affinity constants. Thereby, the chlorine derivative of the fumaroid crotonic acid becomes, in its energy relation, maleinoid to the stereoacid and *vice versa*.

The reason of the inversion of the usual melting-point relations in these acids to their energy-contents is now obvious. The increase by replacing H by Cl is 23° larger in the *trans*- (III) than in the *cis*- β -substance (IV); but this difference is considerably less than that between the melting points of the two crotonic acids (57°). We can now understand the greater solubility of the higher melting acid in water, as this property is directly connected with the larger content of free chemical energy; also, that it gives the lower melting, fumaroid form on heating, and crotonic acid on reduction.

In accordance with the above classification and the tendency to *trans*-addition, is the formation of the higher melting, β -chlorocrotonic acid (IV) from tetrolic and hydrochloric acids.¹

These relations between configurations and affinity constants explain, also, the apparently anomalous results obtained in the reduction of the acids. The lower melting β -chlorocrotonic acid (9.5), as a derivative of allocrotonic acid, should give that acid exclusively, but it yields a mixture containing the fumaroid form in a larger proportion. The energy accompanying the formation of nascent hydrogen suffices to the partial conversion, which would be still greater if the acid had a larger affinity constant, and thus generate a greater intramolecular heat of reaction.² This interpretation is confirmed by the reduction of the lower melting α -chloro-acid (158), which should also yield allocrotonic acid, as here the conversion into crotonic acid is practically complete.³

β -Chloroallocrotonic acid (III) is formed in the action of phosphorus pentachloride on acetoacetic ester, a reaction which is accompanied by the elimination of HCl and the conversion of the carboxyl into the acid chloride group. Free acetoacetic ester, as a saturated derivative, has the stereostructure with the maximum intramolecular atomic neutralization; assuming the *trans*-elimination of HCl from the first product of the reaction, the change is represented by



¹ Friedrich, *Ann.*, 219, 370 (1883).

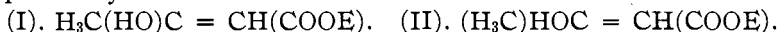
² Wohl, *Ber.*, 40, 2290 (1907).

³ Michael, *J. prakt. Chem.*, [2] 46, 266 (1892).

⁴ The writer suggests the utmost abbreviation, compatible with clearness, in

The formation of β -chloroallocrotonic acid, by trans-elimination of HCl, from allocrotonic dichloride also agrees with the above interpretation.

With the tautomerization of acetoacetic ester, and similar derivatives, the possibility of stereomers arises.



The problem, which of these stereofoms is mal., depends on the relative influence of β -CH₃ and β -OH, and may be answered by the effect of these radicals on the affinity constants of propionic acid. In passing from that acid to (cis) butyric acid the value rises 0.25-0.3, while to (cis) β -hydroxy-^{6 7}propionic acid the increase is 1.7. Evidently, cis-OH, in comparison ^{6 7}to cis-CH₃, is decidedly negative in its action on H and, as the stereomeric relations of acids passes over to the esters, stereostructure (I) must represent the mal. form. The difference in the values of hydroxyl and methyl, however, is considerably less than between chlorine and methyl, in the same positions, which makes it probable that (I) would be easier convertible into (II) than allo- β -chlorocrotonic acid is into β -chloroallocrotonic acid; indeed, enol-acetoacetic ester may consist of a mixture in which the fum. form (II) predominates.

Stereo enol-acetoacetic esters are, as yet, unknown but their *O*-methyl derivatives probably exist. Friedrich¹ obtained by the action of sodium designating organic radicals. Thus, instead of the clumsy Me and Et, etc., the first letter of the alkyl radical should be used. No ambiguity would occur up to the 12th series, except in hexyl and heptyl which could be represented by Hx and Hp, and to denote the alkylenes and alkynes, e and i could be used as suffixes. Atoms or radicals, prefixed or suffixed, to the above abbreviations could indicate substitutions of hydrogen, respectively, additions, and could be used, too, in connection with the Geneva nomenclature. Thus, BH and Bi-2 would represent butane and butine-2, and 2.3-Cl₂-AH or Ae-Cl₂-(2.3) would stand for 2,3-dichloropentane or amylen-(2.3)-dichloride.

To curtail the names of acid radicals by suffixing c in the same way would lead to confusion, owing to the use of Ac for acetyl, and to the names of some of the acids in higher series; it would be preferable to start from Ac as acetyl and form formulas in the way given above; thus, P-AcCl would denote butyryl chloride. In designating aldehydes and acids, the Geneva nomenclature, in connection with the hydrocarbon contractions, could be used.

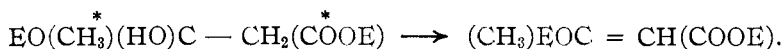
Further, a similar curtailment in designating the various classes of organic derivatives; thus, instead of iso-, sec-, tert-, quart-, keto-, stereomeric, it would be equally significant to use i-, s-, t-, q-, k-, st-. The employment of Ph for phenyl could be usefully extended to Tl, Xl, Npl, etc., for tolyl, xylyl, naphthyl, etc., and e and i, used as suffixes, to characterize further unsaturation; thus, Phe(NH₂)₂ would denote phenylenediamine.

These suggestions are regarded as tentative and can doubtlessly be much improved. Some system of this sort would, after a short experience, convey a quicker and more definite impression of the chemical nature of the compound, especially when of a complicated structure, than the one in present use.

¹ *Ann.*, 219, 322 (1883).

ethylate on both β -chlorocrotonates, in the heat, the same β -ethoxycrotonate.¹ Later, Enke² got a β -methoxycrotonic ethyl ester by the action of sodium methylate on β -chloroallocrotonic ester, and v. Pechmann³ an *O*-methyl derivative by the action of diazomethane on acetoacetic ester. The latter product showed a higher boiling point, but on saponification with alkali it yielded the same β -methoxycrotonic acid. Von Pechmann called this product " β -methoxy-cis-crotonic ester" and gave it the configuration $(\text{CH}_3)_2\text{H}_3\text{COC} = \text{CH}(\text{COOE})$. Apart from the fact, that the separate existence of these bodies seems still open to question, owing to the unusually facile stereomerization of the acid by the alkali, this stereostructure cannot be correct. $\overset{6}{\text{C}}\overset{7}{\text{H}_3}$ is decidedly positive to $\overset{6}{\text{C}}\overset{7}{\text{O}}\overset{8}{\text{CH}_3}$

in its influence on H, and the mal. configuration is $\text{H}_3\text{C}(\text{H}_3\text{CO})\overset{\text{I}}{\text{C}} = \text{CH}(\text{COOE})$. This grouping agrees with the higher boiling point, as a derivative of (trans) crotonic ester, and with the instability of the corresponding acid; it is in accord with the formation of Friedrich's ethoxycrotonic ester, by the action of HCl on a mixture of alcohol and acetoacetic ester,⁴ which proceeds with the preliminary addition of alcohol to the keto-carbonyl, and then by trans-elimination of water and shifting of the α -hydrogen.



Stereomeric thio-derivatives have been obtained by Autenrieth⁵ in the action of sodium ethylmercaptide, and sodium phenylsulfinate, on the β -chlorocrotonates. Accepting direct substitution, and the Wislicenus configurations, the stereostructures $(\text{CH}_3)\text{ES}$, or $\text{PhSO}_2, \text{C} = \text{CH}(\text{COOH})$ were given to the higher melting, more soluble products obtained from allo- β -chlorocrotonic acid (94°). As PhSO_2 is a very strong negative radical, and ES- much more so than EO-, the mal. forms must be $\text{H}_3\text{C}(\text{ES}, \text{or PhSO}_2)\overset{*}{\text{C}} = \text{CH}(\text{COOH})$, and products of these stereostructures must be formed as the result of an addition and then elimination process in the reactions. This classification agrees with all the chemical properties of these substances; for instance, the silver salt of the fum. β -thioethoxycrotonic acid⁶ splits off Ag_2S more readily than the stereomeric salt, which is characteristic of the trans-relation,⁷ and the mal. phenylsulfon-acid is converted by heat into the fum. modifi-

¹ An explanation will be given under substitution in the second communication.

² *Ann.*, **256**, 209 (1890).

³ *Ber.*, **28**, 1627 (1895).

⁴ Curtiss, *Amer. Chem. J.*, **17**, 438 (1895).

⁵ *Ann.*, **254**, 222 (1889); **259**, 332 (1890); *Ber.*, **30**, 1629 (1895).

⁶ Wrongly called thioethyl-crotonic acid.

⁷ Michael, *J. prakt. Chem.*, [2] **52**, 311, 326 (1895).

cation. Escales and Baumann¹ prepared β -dithiophenoxy-butyric ester, by condensation of phenyl mercaptane and acetoacetic ester, which with alkali loses phenyl mercaptane, and gives the mal. β -thiophenoxycrotonate. Accepting saponification as the first step, the salt thus formed should be a derivative of the more acidic configuration, *i. e.*, H_3C , $\text{PhS}(\text{PhS})\overset{*}{\text{C}} - \text{CH}_2(\overset{*}{\text{COONa}})$, which, with loss of PhSH , should give the salt of the more acidic, mal. stereoacid.

The second law of thermodynamics demands that in all addition processes the chemical system should strive to realize the maximum increase of entropy, *i. e.*, the formation of the fumaroid product, but the conditions with stereomeric derivatives are far more complicated than in ordinary reactions: first, because the reagent may act catalytically, before or coincident with the addition, and convert completely or to a more or less extent, the maleinoid into the fumaroid form; and, secondly, because of the undoubted existence in all unsaturated, organic derivatives of a powerful force that tends to cause trans-additions. This directive trans-force, which finds no expression in our present stereochemical theory,² involves a hindrance, since an intramolecular shifting of atoms or groups, or their gyration about the axial carbons, must take place, which the system must have sufficient energy to overcome in order to permit trans-addition.

Phenylpropionic acid gives by the mild action of molecular hydrogen a mixture of the maleinoid cinnamic acids, that is, the reaction proceeds by cis-addition, because the system has not sufficient free energy to cause the shifting or gyration. But the fumaroid cinnamic acid is formed through the extra energy accompanying the formation of nascent hydrogen. On the other hand, molecular hydrogen and acetylene dicarboxylic acid, whose content in free energy finds expression in an affinity constant about that of sulfuric acid, would, probably, yield fumaric acid.

Evidently, the use of addenda with large content of free energy should favor trans-addition, which, indeed, takes place in all additions of halhydric to acetylenic acids; that the latter bodies with bromine give mixtures of the stereomeric addition products, in which the compounds formed in the trans-process predominate, is undoubtedly connected with the decreasing difference between the energy-contents of the mono-, and di-halogen derivatives. For instance, if the α -H of $\text{H}_3\text{C}(\text{Cl})\text{C} = \text{CH}(\text{COOH})$, and that of $(\text{H}_3\text{C})\text{C}(\text{Cl}) = \text{CH}(\text{COOH})$, is replaced by Cl, the relative difference between the affinity constants should decrease in the new acids, for, in

¹ *Ber.*, 19, 1790 (1886); Autenrieth, *Loc. cit.*

² Pfeiffer's attempt (*Z. physik. Chem.*, 48, 40 (1904)) to explain trans-additions, by an inherently improbable assumption, failed, for, apart from various other reasons, cis-additions also take place, and such processes are incompatible with his hypothesis.

the first instance, the α -Cl is in the cis-place to H₃, while, in the other case, it is cis only to the comparatively, subordinate H. Since α -Cl has a great influence on the acidic hydrogen, its effect to increase the constant must be greater in the latter than in the first substitution.

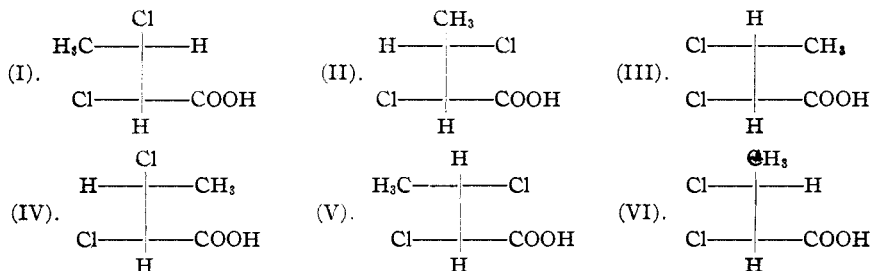
The same directive trans-force prevails in additions to ethylenic derivatives. For instance, Werner¹ assumed the trans-process in the addition of bromine to maleic acid, to explain the close chemical relationship between the addition product and racemic acid. This assumption conforms not only to the energy-conditions, and the molecular rotary power of the isoamyl esters,² but the racemic nature of the dibromo acid has recently been experimentally proven.³

In the addition of bromine to tetrolic acid a mixture of the stereomeric dibromides are formed,⁴ in which the lower melting form is found in larger proportion. Trans- and cis-additions give the following configurations:



By trans-addition, evidently, the more acidic, maleinoid bromo acid (I) is formed, and this lower melting (94°) and more soluble form, loses bromine by trans-elimination⁵ more readily than the higher melting, fumaroid acid⁶ (120°), and is converted into it by the action of hydrobromic acid.⁷

Trans-addition of chlorine to crotonic and allocrotonic acids and rotation, permits the following configurations:⁸



¹ *Lehrb. d. Stereochemie*, 226 (1904).

² Michael, *Amer. Chem. J.*, **39**, 15 (1908).

³ McKenzie, *Chem. Soc.*, 101, 1196 (1911); Holmberg, *Svensk Kem. Tidskr.*, No. 5 (1911).

⁴ Michael, *Ber.*, **34**, 4221 (1901).

⁵ The former rule, IX (Michael, *J. prakt. Chem.*, [2] **52**, 346 (1895)) that a fumaric acid loses halogen, or halhydric acid, easier than the corresponding malic form should be changed to trans- taking place more readily than cis-elimination.

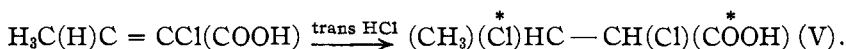
⁶ Michael and Mighill, *Ber.*, **34**, 4225 (1901).

⁷ Pinner, *Ibid.*, **28**, 1877 (1895).

⁸ With cis-additions these configurations are reversed, *i. e.*, (I), (II) and (III) result from allocrotonic acid, and (IV), (V) and (VI) from crotonic acid. The α -H offers the least hindrance to migration (Michael, *J. prakt. Chem.*, [2] **60**, 361 and 368 (1899)).

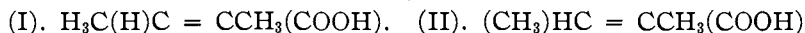
The most acidic of these stereomers should be (II) and (V), since in them chlorine is in the cis-position to the acidic hydrogens; further, (II) should be more acidic than (V), because in the latter chlorine is cis to $\overset{4}{\text{C}}\overset{5}{\text{H}_3}$, while in the former it is cis to H. Since in such saturated derivatives the affinity constants represent the most acidic of the possible configurations, it is evident that the determination of the constants of the stereomeric crotonic dichlorides should decide the nature of the additive process. It has been shown¹ that the constant of the dichloride from crotonic acid (820) is larger than that from allocrotonic acid (607), and it follows from these values that the addition is a trans-process.

The configuration of allocrotonic dichloride given above is confirmed by the formation from α -chlorocrotonic acid.²



Tiglic and Angelic Acids.

The substitution of H by $\overset{5}{\text{C}}\overset{6}{\text{H}_3}$ in a fatty acid invariably proceeds with reduction of the K value; accordingly, in tiglic (I) and angelic (II), or allotiglic acids,



which are formed in this way from crotonic and allocrotonic acids, there is a decrease from 2 and 6-7 to 0.9 and 5.³

In agreement with the configurations are all the physical and chemical properties of these stereomers. Interesting is their behavior towards bromine in the dark and in sunlight. In the dark they yield separate dibromides; in sunlight, tiglic acid gives the same dibromide as in the dark, and also a small amount of angelic dibromide, while angelic acid also yields to a greater or less extent, according to conditions, tiglic dibromide with angelic dibromide.⁴

The configuration relations in the trans-addition of bromine to these acids are similar to those discussed above in the addition of chlorine to the crotonic acids. The behavior of angelic acid towards bromine may now be explained; in the dark, the energy in the "polymolecule" of halogen and acid is insufficient to convert it into tiglic acid, but with the assistance of actinic, or of heat energy, stereomerization proceeds the addition to a more or less extent.

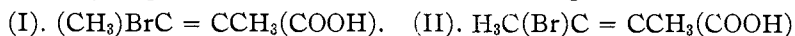
¹ Michael and Bunge, *Ber.*, **41**, 2909 (1908).

² Michael and Schulthess, *J. prakt. Chem.*, [2] **46**, 259 (1892).

³ The greater proportionate decrease in tiglic acid (I) is probably due to the fact that the energy in CH_3 is used up to a larger extent by being cis to CH_3 than to H.

⁴ Fittig, *Ann.*, **259**, 29 (1890); **273**, 127 (1893); J. Wislicenus, *Ann.*, **272**, 7 (1893); **274**, 99 (1893).

Trans-elimination of HBr from tiglic and angelic dibromides leads, whether by migration of CH_3 or Br, to the following stereoforms:



Although angelic dibromide yields a bromo derivative (II) of (fum.) tiglic acid, it evidently represents the mal. modification and, accordingly, it is more soluble in water than bromoangelic acid (I). Its melting point (101°) is slightly higher than that of the latter acid (95°). Crotonic acid melts 57° higher than allocrotonic acid, and the introduction of Cl in the cis-, respectively, in the trans-position to COOH , reduces the difference to 34° , respectively, 23° . When the much smaller difference in the melting points of tiglic (65°) and angelic (45°) acids is taken into consideration, it is evident that the slight difference between that of bromoangelic and bromotiglic acids might have been expected. These configurations of the bromo acids are confirmed by the behavior of the potassium salts at 100° , since only that of bromoangelic acid (I) decomposes easily into butine-2 and CO_2 , which agrees with the trans-position of Br and COOK .¹

Influence of Ethylenic Unsaturation on Affinity Constants.

This subject has been investigated recently by Fichter and Pfister,² who find that the values for α, β, Δ -aliphatic acids are only slightly higher, indeed in the pentenic series, less, than those of the corresponding saturated derivatives, and that they increase in the β, γ, Δ -acids to fall with further removal of the unsaturation from the carboxyl group. They compare these relations with the great increase in the introduction of halogen in the α - and then the progressive decrease in the β - and γ -positions, and conclude that double linkage cannot be considered a negative substituent, although in other groups of derivatives it apparently acts as such.³

The effect of the above unsaturation is to increase the affinity constant in three ways: First, it removes basic hydrogen; secondly, the axial carbons and the atoms or groups joined to them become relatively more negative or less positive, and, finally, the unsaturated, axial carbons and the atoms in cis-position to carboxyl, spacially approach the acidic hydrogen. The large increase in the affinity constant with such unsaturation follows from these relations; also, that the difference between the values of two homologous, saturated acids is always less than those of the corresponding ethylenic acids with similar configurations.

To explain the experimental observations with these acids, it is necessary to assume that the hydrogen unsaturation of a carbon increases the

¹ Michael, *J. prakt. Chem.*, [2] 52, 311 (1895).

² *Ann.*, 334, 201 (1904).

³ See Henrich, *Theorien Org. Chem.*, 1912, pp. 83-103. For a criticism of the views of Henrich and Vorlaender on this subject, and for interpretations founded on the energy and affinity relations, see Michael, *J. prakt. Chem.*, [2] 68, 496 (1903); *THIS JOURNAL*, 32, 1002 (1910).

constant much more than the removal of a hydrogen in the same position as the carbon to H. The great increase in the affinity constants accompanying unsaturation makes such an assumption very probable; for instance, the presence of two, completely unsaturated carbons in the fifth position to the acidic hydrogens of acetylene dicarboxylic acid, coupled with the spacial approachment of the carboxyls, give it approximately the acidity of sulfuric acid.¹

The supposed contradictions in the negative influence of the ethylenic bond are partly due to the comparison of the values of dissimilar configurations. Although the constant of the fum. crotonic acid (2) is only slightly higher than that of (cis) butyric acid (1.5), the much larger value of the really comparable (cis) allocrotonic acid (6-7) plainly shows the very considerable negative influence of the unsaturated radical.² It is, also, not permissible to conclude, with Fichter, from the constants of crotonic (2) and vinylacetic (3.8) acids that β, γ - has a greater effect than α, β -unsaturation, since a comparison of the value of the latter acid with that of allocrotonic acid (6-7) leads to exactly the opposite conclusion. The true relations appear to be that such a β, γ, Δ -derivative has a larger value than the isomeric α, β -acid of the trans-, but smaller than that of the cis-series. With trans- β, γ - and γ, δ -pentenic acids, omitting the atoms common in each group, we have the following relations to H:

$$\begin{aligned} \beta, \gamma: & \overset{5}{\Delta C} + \overset{7}{\text{trans-C}} + \overset{7}{\text{cis-H}} + \overset{8}{\text{trans-H}_2} \\ \gamma, \delta: & \overset{5}{C} + \overset{7}{\Delta\text{-C}} + \overset{8}{\text{cis-H}} + \overset{7}{\text{H}} + \overset{7}{\text{H}} \end{aligned}$$

The influence of the carbons and of the cis-hydrogen evidently favors the acidity constant of the β, γ -acid, while the remaining hydrogens act in the opposite direction; but, with the relatively greater influence of the carbons, it is evident that it should possess the larger constant.

With α, β -pentenic acid stereoisomerism is possible and the one known substance is fum., since the constant (1.5) is less than that of crotonic acid, and a reduction of the value is only possible by substitution of trans- $\overset{7}{\text{H}}$ by $\overset{7}{\text{C}}\overset{8}{\text{H}_3}$.

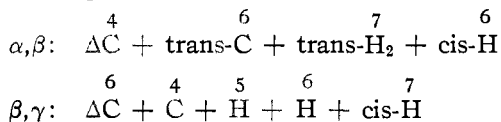
Fichter has called attention to an apparent anomaly in this series in that the constant of the α, β -acid (1.5) is less than that of the corresponding saturated acid (1.6). This unusual relation is the result of a comparison of acids with unlike configurations. In the change from (cis) butyric

¹ Ostwald, *Z. phys. Chem.*, **3**, 382 (1889).

² The decided negative influence is also apparent in the values of the comparable propionic (1.3) and acrylic (5.6) acids.

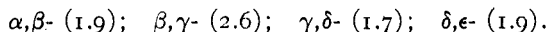
(1.52) to (cis) valeric acid (1.59)¹ the replacement of a cis-H by $\overset{7}{\text{C}}\overset{7}{\text{H}}_3$ increases the constant slightly, while from (trans) crotonic (2) to (trans) α,β -pentenic acid a decrease takes place. The cis-form of α,β -pentenic acid, whose stereostructure is like that of valeric acid in dilute solution, would show a much larger constant, probably 7-8.

The only known β,γ -pentenic acid also represents a fum. substance, as it may be derived from vinylacetic acid (3.8), and shows a smaller constant (3.3). Comparing the α,β - and β,γ -acids, as shown above, leads to the following relations:



In the β,γ -acid the carbon atoms exert a decidedly greater negative, cis-H, in place of cis-H a less positive, and $\overset{5}{\text{H}} + \overset{6}{\text{H}}$ a positive, but evidently a smaller effect. In this series, the β,γ -acid has, therefore, the larger constant.

The constants of the acids in the hexenic series are



All these values are higher than that of the saturated capronic acid (1.4). The comparatively low values of the first three acids show that they are fum. modifications, and the relations of their constants to each other agree with the explanations given above for the corresponding pentenic acids.

A striking anomaly is shown in that α,β -pentenic acid (1.5) has a smaller constant than α,β -hexenic acid (1.9), that is, the introduction of $\overset{8}{\text{trans-CH}_3}$ has an effect opposite to that of $\overset{6}{\text{CH}_3}$ and $\overset{7}{\text{CH}_3}$ in the trans-relation. This rise cannot be explained by assuming a cis-configuration for the hexenic acid, since its value would be considerably higher than that of the acid in question. It seems probable, that it is due to a periodicity in the spacial positions of atoms in trans-positions, like there

¹ These are the values given by Franke (*Z. physik. Chem.*, 16, 480 (1895)), who used acids prepared by fractionation from "Kahlbaum's" purest products. It is unfortunate that physical chemists are under the delusion that really pure preparations can be separated in that way from products that are evidently mixtures. Billitzer (*Monatsh.*, 20, 666 (1899)) obtained his valeric acid (1.61) through malonic ester, but we know now that it is impossible to completely separate the mono- from the dialkyl malonic derivatives, except by chemical means (Michael, *J. prakt. Chem.*, [2] 72, 537; *Ber.*, 38, 2093 (1905)). The determinations of standard affinity constants would give data of great theoretical importance; Ostwald's values were obtained largely from more or less impure acids. These remarks unfortunately apply to the majority of physico-chemical, organic investigations.

is in cis-positions; and, that trans-C⁸ is spatially nearer to H than trans-H⁹, *i. e.*, its effect is comparable to that of cis-CH₃^{6 7}. This increase, in connection with the decrease in passing from valeric to capronic acid, explains why the constant of α, β -hexenic acid is higher than the corresponding (cis) saturated acid, instead of being lower, as in the fifth series.

The substitution of α -H in α, β -pentenic acid (1.5) by methyl introduces^{5 6} CH₃ and reduces the constant to 1, which is approximately the same percentage as in the analogous change from acetic to propionic acid. The further conversion to butyric acid (1.54) brings in the negative CH₃^{6 7}, and, analogously, the change from α -methyl- to α -ethyl-pentenic acid causes an increase (2). An exception occurs in that the introduction of^{6 7} α -CH₃ in β, γ -pentenic acid (3.3) reduces the constant to 3, while the larger value of the α -ethyl derivative (3.4) agrees with theory; as does, that^{7 8} α -CH₃ introduced into γ, δ -pentenic acid causes only a very slight change. The most marked discrepancies from theory are shown by the acids formed in the substitution of cis-H in α, β -pentenic acid by CH₃^{6 7}, and in the β, γ -⁷ derivative, of cis-H by that radical, when the constants are lowered, instead of increased.¹

Dibasic Unsaturated Acids.²

Ostwald³ determined the constants of maleic and fumaric acids and their methyl derivatives and found that the value of mesaconic (K_1 79) is somewhat less than that of fumaric (K_1 93), while that of citraconic (K_1 340) is only about one-third of that of maleic (K_1 1170) acid. Since the methyl group reduces the constant, and is nearer to carboxyl in mesaconic than in citraconic acid, Ostwald expected that the relative changes in the relations would be reversed. In this problem, the primary factors are the positions of the introduced atoms to

¹ Fichter and Mueller, *Ann.*, **348**, 258 (1906).

² The hindrance to rotation in succinic acid should be greater than in monobasic, saturated acids, and it probably exists mainly in the trans-form in solution. This conclusion agrees with the small affinity constant (K_1 6.6), which, for the cis-acid, should not be less than K_1 25. Bruni's observation, that succinic and fumaric methyl esters have similar (trans) stereostructures also confirms this conclusion, as esterification represents a partial neutralization of the negative, acidic energy and, unless there is a decided hindrance to rotation, the succinic ester should assume the maleinoid configuration. This relative stability of the fum. succinic acid is connected with the properties of the stereomeric alkyl derivatives, a subject which will be discussed in a later paper.

³ *Z. physik. Chem.*, **3**, 383 (1889).

the acidic hydrogens and the oxygens; the indirect influence of the latter atoms on the change in the affinity constant is, evidently, much greater when the carboxyls are in *cis*-, than in *trans*-position. When the new influences coincide in their effect, then there should be a decided difference, otherwise, they should neutralize each other to a more or less extent and the change should be relatively much smaller. The replacement of $\overset{6}{\text{trans-H}}$ by $\overset{6}{\text{CH}_3}$ in maleic acid introduces $\overset{6}{\text{trans-CH}_3}$ to one of the acidic hydrogens and $\overset{5}{\text{CH}_3}$ to the other. Each change reduces the negative energy of the acidic hydrogens and, also, that of the oxygens, which, owing to their being in *cis*-position to each other, is a considerable factor in the great decrease.

That the primary constant of fumaric acid (93) is so much less than that of maleic acid (1170) is due to the much greater reduction of the negative energy of the oxygens by hydrogen in the *cis*-, than in *trans*-position; further, to the *trans*-relationship of these oxygens and, finally, that the Δ -carbons are less negative. The values for bromofumaric (K_1 1800) and bromomaleic acid (K_1 7000)¹ lie much closer together, which is due to the replacement of a H by an atom that, for special reasons, increases the negative energy at the acidic hydrogen of the fum. body to a far greater extent than it does in the mal. derivative. Corresponding energy changes occur with the further substitution of H by halogen.²

Ethyl-maleic acid may be derived from citraconic acid by replacing a $\overset{6}{\text{trans-H}}$ of the methyl group by $\overset{5}{\text{CH}_3}$, which introduces $\overset{6}{\text{CH}_3}$ and $\overset{7}{\text{trans-CH}_3}$ to the acidic hydrogens, and $\overset{6}{\text{CH}_3}$ and $\overset{7}{\text{trans-CH}_3}$ to the oxygens. $\overset{7}{\text{CH}_3}$ increases the constant somewhat, but $\overset{7}{\text{trans-CH}_3}$ causes a greater decrease, which is enhanced by the same influence on the oxygens. The K_1 constant falls from 340 to 238.

The corresponding change in mesaconic acid introduces $\overset{6}{\text{CH}_3}$ and $\overset{7}{\text{cis-CH}_3}$ to the acidic hydrogens and $\overset{5}{\text{CH}_3}$ and $\overset{6}{\text{cis-CH}_3}$ to the oxygens. $\overset{7}{\text{CH}_3}$, also, probably, $\overset{7}{\text{cis-CH}_3}$, increase the constant; $\overset{5}{\text{CH}_3}$ reduces the negative energy of the oxygens, which is offset by $\overset{6}{\text{cis-CH}_3}$. As, with *trans*-carboxyls, the latter influences are subordinate and the (K_1) value increases methyl-fumaric acid (79 to 94). The change from ethyl-, to propyl-mesaconic acid brings in $\overset{7}{\text{CH}_3}$ and $\overset{8}{\text{cis-CH}_3}$; these influences are similar to those in passing

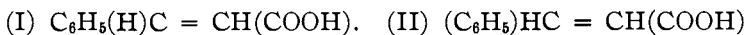
¹ Holmberg, *J. prakt. Chem.*, [2] 84, 162 (1911). The smaller value of dibromomaleic acid (K_1 3700) indicates that it exists partly as anhydride in dilute aqueous solution.

² Walden, *Z. physik. Chem.*, 8, 479 (1891); Holmberg, *Loc. cit.*, p. 166.

from butyric to valeric and from valeric to capronic acids, where a very slight increase and slightly greater decrease occur. The value (K_1) falls from 94 to 93.

Cinnamic Acids.

That the stereomeric relations in the cinnamic series are closely related to those in the crotonic was proven experimentally,¹ and the attempt of J. Wislicenus² to change this relationship was afterwards abandoned.³ All the properties of cinnamic (3.5) and allocinnamic (14.2) acids conform with the configurations



and the affinity constants show that C_6H_5 is decidedly negative to H in the cis-position, but positive to it in the trans-place. Cinnamic acid and Cl_2 in the dark,⁴ or in light free from actinic rays,⁵ yields the mal. dichloride (84°); in sunlight, the high-melting (163°) fum. product.⁶ These results are comparable, and the configurations are similar to those discussed above with crotonic acid, only, owing to the characteristic greater hindrance to stereomerization in the latter series, actinic sunlight not cause such a change, which may be effected, however, by heating crotonic alldichloride with HCl.⁷ Unfortunately, the stereomeric cinnamic dichlorides decompose somewhat into chlorostyrols in dilute solution, so that a determination of their affinity constants is impossible,⁸ but it follows conclusively from other properties, that the lower melting dichloride is the mal. acid; *i. e.*, its formation from cinnamic acid and, therefore, that of the fum. dichloride from allocinnamic acid,⁹ proceed by trans-addition.

In the dark, cinnamic acid and bromine yield the high melting, fum. dibromide (201°) and only 10% of the mal. stereomer (91°), but with the methyl and ethyl esters the proportion of latter products increase to about one-third, respectively, one-half.¹⁰ To effect trans-addition the hindrance due to the shifting of an atom or group has to be overcome, and the decreased yield of allo-addition product with bromine over that with chlorine may be connected with its smaller content of free energy. Further, the increase in allo-product with the esters may be due to the decrease of free energy in the carboxyl accompanying esterization, which should

¹ Michael, *Ber.*, 19, 1378 and 1384 (1886); 20, 550 (1887).

² *Rauml. Anordnung U. S. W.*, 47 (1887).

³ *Ibid.*, 2nd edition, 79 (1888).

⁴ Liebermann and Finkenbeiner, *Ber.*, 28, 2235 (1895).

⁵ Michael and Smith, *Amer. Chem. J.*, 39, 16 (1908).

⁶ Erlenmeyer, *Ibid.*, 14, 1867 (1881).

⁷ Michael and Bunge, *Ber.*, 41, 2912 (1908).

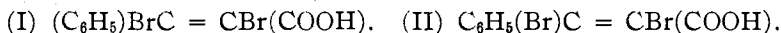
⁸ *Ibid.*, 2913.

⁹ Liebermann and Finkenbeiner, *Ber.*, 28, 2235 (1895).

¹⁰ Michael and Whitehorne, *Ibid.*, 34, 3660 (1901); Michael and Smith, *Am. Chem. J.*, 39, 16 (1908).

lessen the hindrance to rotation; in agreement, is the increased percentage of allo-dibromide with the ethyl over that with the methyl ester. This explanation is confirmed by the behavior of chlorine and bromine towards other unsaturated derivatives. Bromine unites solely by trans-addition with maleic and fumaric acids; with acetylene dicarboxylic acid, where the hindrance to rotation is increased, also by the cis-process. Crotonic acid and halogens unite by trans-addition, but, with tetrolic and bromine, both processes occur simultaneously, while with chlorine apparently only trans-addition takes place.

Bromine and phenylpropionic acid give a mixture of the stereomeric dibromocinnamic acids.¹



The formation of (II) proceeds by trans-addition and represents the mal. form; as a derivative of cinnamic acid (132°), it has a higher melting point (139°) than the fum. acid (100°), but its mal. character is shown by its conversion by bromine into (I), and the configuration of that acid (I) by its conversion by condensation into dibromindone.² Chlorine and phenylpropionic acid³ yield a single α,β -dichlorocinnamic acid (120°), which, by its comparatively low melting point, and through its conversion into dichloroindone, is characterized as the fum. derivative (corresponding to (I)). Since bromine, under the conditions of the addition, is able to catalytically convert the mal. (I) into the fum. (II) product, it is not improbable that some of the latter substance is thus formed indirectly. And the abnormal formation of only the fum. dichloride may be due to the chlorine, with its greater energy, entirely stereoisomerizing the first-formed mal. addition product.⁴

The addition of HBr to phenylpropionic acid yields two β -bromocinnamic acids,⁵ melting at 160 and 134° , but it will be shown in a subsequent paper that the lower melting acid is formed secondarily by the catalytic action of the mineral acid on the higher melting stereomer, from which it may also be obtained by heating.⁶ The relations, excepting the catalytic transmutation, agree with those of the chlorocrotonic acid formed by trans-addition of HCl to tetrolic acid. Here, too, the mal. character of the higher melting acid is shown in the greater solubility in water, and its high melting point conforms with its derivation from cinnamic acid. On the other hand, a most marked difference exists in the behavior of these bromo acids on

¹ Roser and Haselhoff, *Ann.*, **247**, 138 (1888).

² Roser and Haselhoff, *Loc. cit.*

³ Nissen, *Ber.*, **25**, 2665 (1892).

⁴ It would be of interest to study these reactions in the dark.

⁵ Stockmeier, Dissertation, p. 73; Michael and Browne, *Ber.*, **19**, 1379 (1886); **20**, 552 (1887).

⁶ Erlenmeyer, *Ann.*, **287**, 24 (1895).

reduction, since the 159° melting β -acid yields allocinnamic acid,¹ whereas, according to its configuration, it should give the fum. acid; also, the ease with which it decomposes into phenyl acetylene, and a smaller velocity of elimination of HBr, are opposed to the stereostructures given above, and to the relation of the corresponding halogen acids in the crotonic series.

An attempt² to determine the affinity constants of the β -bromo acids was without success, but those of the corresponding chloro-acids are known.³ The higher melting acid is the mal. derivative, but its affinity constant (28) is only slightly higher than that of the fum. acid (27.2). This relation shows that the increase in the affinity constant of acrylic acid (5.6) caused by cis- C_6H_5 , less the decrease by trans- C_6H_5 , is only slightly greater than the increase due to cis- C_6H_5 plus that of trans-Cl, and the relation is reflected in the approximation of their melting points and solubilities in water. It is remarkable, that the β -chloro- and β -iodo-cinnamic acids, corresponding to 160° melting β -bromo derivative, yield in the same method of reduction cinnamic, instead of allocinnamic acid.⁴ No other problem in the field of stereomeric configurations is so perplexing and enigmatical as that of the β -halogen cinnamic acids, and the recent experimental results have added to the difficulties awaiting a satisfactory solution.

In the next paper, the relations between these configurations of unsaturated acids and their other physical and chemical properties will be treated

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO.]

THE PREPARATION OF PHENYLETHYLBARBITURIC ACID.⁵

BY MARY RISING AND JULIUS STIEGLITZ.

Received March 19, 1918.

Phenylethylbarbituric acid is a member of the ureid group of hypnotic drugs, of which diethylbarbituric acid, introduced as "veronal" and now known as "barbital,"⁶ is the best known and most important representative. Phenylethylbarbituric acid, "phenylbarbital,"⁷ introduced as "luminal,"

¹ Liebermann and Scholz, *Ber.*, **25**, 950 (1892).

² Michael and Bunge, *Ibid.*, **41**, 2913 (1908).

³ Millikin, Dissertation, Leipsic (1890).

⁴ Michael and Whitehorne, *Ber.*, **34**, 3659 (1901).

⁵ The work reported on in this article will form part of the dissertation to be submitted to the University of Chicago by Miss Rising in part fulfillment of the requirements for the doctorate degree.

⁶ The official name of this drug, adopted by the U. S. Federal Trade Commission in the issuance of licenses for its manufacture, is "barbital." The reasons for the adoption of new official names for the licensed drugs and for the recommendation that these names be generally used by chemists and physicians in this country are presented by one of the authors in the *J. Am. Med. Assoc.*, **70**, 536 (1918).

⁷ "Phenyl-barbital" is the name for phenylethylbarbituric acid, which will be used in the issuance of licenses for its manufacture in this country.