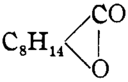
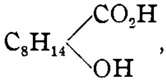
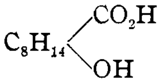
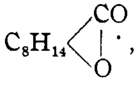
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS.]

MOLECULAR REARRANGEMENTS IN THE CAMPHOR SERIES. X. CAMPHOLYTIC ACID AND RELATED COMPOUNDS. WALDEN'S REARRANGEMENT.

BY WILLIAM A. NOYES AND RALPH S. POTTER.

Received May 17, 1912.

By the replacement of one or the other carboxyl of camphoric acid with the amino group, through the amide, by Hofmann's reaction, two amino acids are obtained; aminocamphonanic acid[1] and aminodihydrocampholytic acid.[2] 3-Aminocamphonanic acid gives by treatment with nitrous acid, directly or indirectly, laurolene, C_8H_{14}, and lauronolic acid, $C_8H_{13}CO_2H$, in both of which one methyl group has shifted from the β- to the γ-position with reference to the original position of the carboxyl and the three methyl groups are combined with three different carbon atoms. Isocampholactone,  $C_8H_{14}\langle{}^{CO}_{O}\rangle$, whose structure is still uncertain, is also formed. In campholactone, which is formed on warming lauronolic acid with dilute acids, the methyl groups are probably also in the 1,2,3-positions, though this has not been definitly proved. Recently it has been shown[3] that one of the products of the decomposition, camphonolic acid,  $C_8H_{14}\langle{}^{CO_2H}_{OH}$, retains the grouping of the methyl groups which is characteristic of camphoric acid, but it is now clear that in the formation of the principal decomposition products from aminocamphonanic acid a methyl group shifts from one carbon atom to another.

In contrast with the variety of products formed by the decomposition of aminocamphonanic acid, only three substances have, hitherto, been reported as found when aminodihydrocampholytic acid is treated with nitrous acid. These are: *trans*-hydroxydihydrocampholytic acid,[4]  $C_8H_{14}\langle{}^{CO_2H}_{OH}$, campholytolactone,[5]  $C_8H_{14}\langle{}^{CO}_{O}\rangle$, and campholytic acid,[6] $C_8H_{13}CO_2H$.

---

[1] Called by Hoogewerf and Van Dorp aminolauronic acid (see *Am. Chem. J.*, 16, 501 (1894)). The name here given is suggested by Professor Bredt in the interest of a more rational nomenclature.

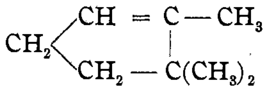
[2] *Am. Chem. J.*, 16, 503 (1894).

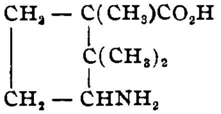
[3] THIS JOURNAL, 34, 62 (1912).

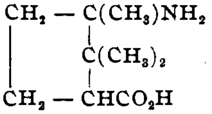
[4] *Am. Chem. J.*, 17, 424 (1895); 24, 286 (1900).

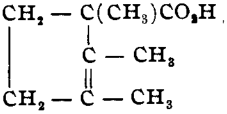
[5] *Ber.*, 33, 2938 (1900).

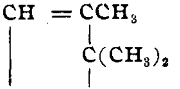
[6] *J. Chem. Soc.*, 63, 498 (1893); *Am. Chem. J.*, 16, 505 (1894); *Ber.*, 33, 2939 (1900).

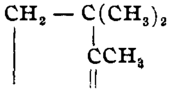
It has now been shown that isolaurolene,  is also formed, but, while the nitroso derivative of the anhydride of aminocamphonanic acid is decomposed on shaking with a solution of sodium hydroxide with the formation of 30% of its weight of laurolene,[1] the nitroso derivative of the anhydride of aminodihydrocampholytic acid when decomposed in the same manner gives only about 3% of its weight of isolaurolene. There can be little doubt that this difference in conduct is closely connected with the shifting of the methyl group which occurs in the formation of laurolene. Either the vibrations in the molecule which accompany the transfer of the group cause the release of the carboxyl group at the same time, or it may be that the double union from the β-carbon atom has a similar effect to that which the union with oxygen in the β-position has in acetoacetic ester, in lessening the affinity of the carboxyl for the carbon atom to which it is united. It is also probable that the grouping in which four carbon atoms are united to these same carbon atoms is not very stable. This last factor is probably involved in the shifting of the methyl group, also. These relations will be more easily understood from an inspection of the formulas of the two amino acids, and of lauronolic, campholytic and isocampholytic[2] acids.


3-Aminocamphonanic acid.


Aminodihydrocampholytic acid.


Lauronolic acid.


Campholytic acid.


Isocampholytic acid.

In previous papers[3] it has been assumed that hydroxydihydrocampho-

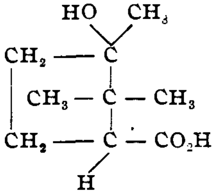
---

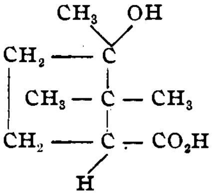
[1] This Journal, 31, 671 (1909).

[2] This acid has been variously called isolauronolic (Koenigs and Hoerlin, *Ber.*, 26, 814 (1893)), camphothetic (Walker, *J. Chem. Soc.*, 63, 504 (1893)), β-campholytic and isocampholytic acid (*Am. Chem. J.*, 17, 430 (1895)). As was pointed out by one of us *Am. Chem. J.*, 17, 430 (1895)) some years ago, the name isolauronolic is undesirable because it obscures the relation to campholytic acid. The names α- and β-campholytic acids, which have been used by a number of authors as well as ourselves, use the Greek letters with reference to an accidental order of discovery and not with reference to structure. While there is considerable authority for such a use of the letters, it seems to us much better to confine their use to the designation of structure. For these reasons isocampholytic acid seems to be the best of the names which have been proposed. Professors Perkin, Aschan, and Bredt have all kindly agreed to this name for the acid (private communication).

[3] *Am. Chem. J.*, 24, 286 (1900); 32, 289 (1904).

lytic acid retains the same configuration as *d*-camphoric acid. The rotatory power of the acid in comparison with that of the amino acid from which it is prepared and that of the bromo acid formed by replacing its hydroxyl by bromine or by the addition of hydrobromic acid to campholytic acid point to such a conclusion. It will be shown in this paper, however, that the isomeric *cis*-hydroxydihydrocampholytic acid when heated with water at 100° readily goes back to campholytolactone, while hydroxydihydrocampholytic acid under the same treatment gives some of *the same lactone*, but chiefly isolaurolene and campholytic acid. It will also be shown that neither the *cis*- nor the *trans*-hydroxydihydrocampholytic acid is oxidized to a ketonic acid by Beckmann's chromic acid mixture, even when strongly acidified. In both cases the hydroxy acid was recovered mostly unchanged from the mixture. As it was shown in a recent paper of this series[1] that camphonolic acid may be easily oxidized to camphononic acid by this treatment, the evidence seems conclusive that both acids contain a tertiary hydroxyl group. Both acids also give isocampholytic acid on warming with dilute sulfuric acid.[2] It seems practically certain, therefore, that the two acids are stereomeric and have the following configurations:


Trans-hydroxydihydrocampholytic acid.


cis-Hydroxydihydrocampholytic acid.

This result forces us to the conclusion that in the decomposition of aminodihydrocampholytic acid by nitrous acid the hydroxydihydrocampholytic acid is formed by a Walden inversion. When we recall that in the decomposition of the isomeric aminocamphonanic acid a methyl group shifts from one carbon atom to another, it does not seem surprising that here the group may shift from one side to the other of the *same* carbon atom. This result seems to have an important bearing on the hypothesis recently proposed by Emil Fischer[3] to account for the Walden rearrangement. It is not clear that the hypothesis which he proposes could help us at all in explaining the transformation of aminocamphonanic acid to lauronolic acid. But if it is not necessary to account for that transformation, we do not see its necessity in explaining the Walden rearrangement.

It is well known, of course, that under the influence of acids or alkalies

---

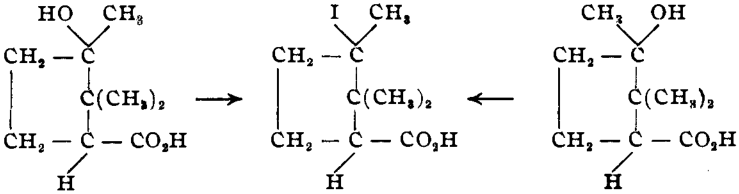
[1] This Journal, **34**, 66 (1912).

[2] *Am. Chem. J.*, **17**, 427, 428 (1895); *Ber.*, **33**, 2939 (1900).

[3] *Ann.*, **381**, 123 (1911).

many optically active compounds are changed to the racemic form. When this condition is reached, in accordance with the principles of chemical equilibrium, the shifting of the groups from side to side does not cease but continues to go on. The racemic form is maintained because the groups shift in one direction just as frequently as in the other. The failure to give a racemic compound under such conditions may be due to either of two causes: first the groups may be so strongly held that they do not shift or the attractions between the atoms may favor one configuration more than the other. The latter seems probable in the case which we are considering. It has been shown[1] that hydrobromic acid adds itself asymmetrically to campholytic acid giving the same compound which is formed by treating *trans*- hydroxydihydrocampholytic acid with hydrobromic acid. It will also be shown below that *cis*-hydroxydihydrocampholytic acid has a very much larger ionization constant than the *trans* acid. Both of these facts indicate that the atomic attractions and repulsions which give rise to the formation of *trans*-hydroxydihydrocampholytic acid are stronger than those which cause the formation of the *cis* acid. There is a close approach here to Michael's positive-negative law.[2]

As will be shown in the experimental part, it seems probable that both *trans*-hydroxydihydrocampholytic acid and the *cis* acid give chiefly the *trans* iododihydrocampholytic when treated with the hydriodic acid. In any case the iodo compound from either acid gives both hydroxy acids, but chiefly the *trans* form (and campholytic acid) when treated with sodium bicarbonate,



It is evident that in one or both of these reactions an incomplete Walden inversion occurs. It would seem that when the hydroxyl group separates from the carbon atom to unite with the hydrogen of the hydriodic acid the vacant affinity of the carbon attracts both the methyl group and the iodine atom and the methyl group rather than the iodine atom takes the vacant place because of the combined attractions and repulsions of all of the other atoms of the molecule. It may also be that in the approach of the molecule of hydriodic acid to the molecule of the hydroxy acid the positions assumed by the hydrogen and iodine atoms are such as to favor the replacement of the methyl by the iodine. Such a view ap-

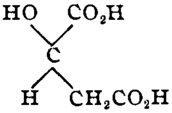
---

[1] *Am. Chem. J.*, **24**, 289 (1900).

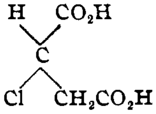
[2] *Ber.*, **14**, 1318; *J. prakt. Chem.*, **37**, 486 (1888); *Ibid.*, **40**, 171 (1889).

proaches the hypothesis of Fischer without assuming, as he seems to do, that the carbon atom is temporarily united to five atoms. It also assumes a temporary grouping very like to the double compounds which have been suggested by Michael.

When only a single asymmetric carbon atom is present, as in the ordinary Walden inversion, the mechanism may be somewhat as follows, in the action of phosphorus pentachloride on malic acid:

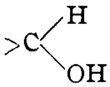


d-Malic acid.



l-Chlorosuccinic acid.

When the phosphorus pentachloride approaches the hydroxyl of the malic acid to react with it, it may well be that the relative positions of the atoms are such that when the hydroxyl group separates from the malic acid it is the hydrogen attached to the adjacent valence of the carbon atom rather than the chlorine atom of the pentachloride which is attracted to the vacant valence. The chlorine atom would then take the place of the hydrogen atom. The well known labile character of hydrogen atoms in carbon compounds favors this interpretation.

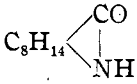
Another possibility is that the phosphorus pentachloride dissociates into phosphorus trichloride and chlorine and that the latter acts as a substituting agent on the hydrogen of the  $>C<^{H}_{OH}$ group, while the phosphorus trichloride combines with the oxygen of the hydroxyl group, leaving the hydrogen of that group to combine with the carbon.

Several other mechanisms could be suggested which would lead to the same final result. The essential points are: first, that molecules tend to approach each other with some definit configuration when they react; second, that some definit sequence is followed in complex actions; and, third, that complex molecules may separate so nearly simultaneously in two or more ways that substitution does not necessarily consist in the recombination of the four parts (here PCl_4, Cl, HO and $CH(CO_2H)CH_2CO_2H$) at first formed. These suppositions appear to us more in accord with our present knowledge than the supposition of a temporary union of a carbon atom with five other atoms. They do not necessarily imply the localization of the affinities of the carbon atom, though we are, on the whole, inclined to the view that there is such a localization.

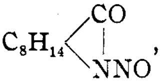
We cannot, of course, be sure that the replacement of a hydroxyl group by chlorine would give a chlorosuccinic acid with a rotation of the same sign, if the original configuration is retained. We can only be sure that an inversion occurs either in the treatment of malic acid with phosphorus pentachloride or in the treatment of the chlorosuccinic acid with silver oxide and water.[1] The advantage of the compounds described in this paper is that the formation or non-formation of a lactone gives independent and quite certain information as to whether an inversion has occurred or not.

Experimental Part.

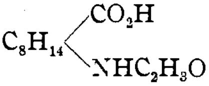
The aminodihydrocampholytic acid required for this investigation was prepared from secondary[2] camphoramidic acid by methods already described,[3] and was purified by solution in cold water and evaporation to crystallization.

Anhydride of Aminodihydrocampholytic Acid,  $C_8H_{14}\left<\begin{matrix}CO\\ |\\ NH\end{matrix}\right.$.—This may be prepared either by distilling the amino acid from a mixture with lime[4] or by itself, or by warming it with acetic anhydride, cooling, diluting with water, nearly neutralizing with sodium hydroxide and extracting with ether. It may be crystallized from petroleum ether. When prepared in this way the rotation was:

$[\alpha]_D = 72.8°$ at 30°; 1 gram in 10 cc. of petroleum ether.

The Nitroso Derivative,  $C_8H_{14}\left<\begin{matrix}CO\\ |\\ NNO\end{matrix}\right.$, is formed when a solution of sodium nitrite is added to a solution of the anhydride in dilute hydrochloric acid. It usually separates at first as an oil which solidifies slowly and it is much less stable than the corresponding derivative of the anhydride of aminocamphonanic acid. It was crystallized from alcohol, slightly diluted, separating in needles which melt at 188–189°, when rapidly heated, but which decompose at a lower temperature if heated slowly.

Calculated for $C_9H_{14}O_2N_2$: N, 15.35; found: 15.15.

Acetyl Derivative of Aminodihydrocampholytic Acid,  $C_8H_{14}\left<\begin{matrix}CO_2H\\ NHC_2H_3O\end{matrix}\right.$ —When the anhydride was prepared by means of acetic anhydride, on solution in dilute hydrochloric acid a relatively small amount of the acetyl derivative of the amino acid separates as a difficultly soluble compound. It may be crystallized from dilute hydrochloric acid or from alcohol and melts at 218°.

Calculated for $C_{11}H_{19}O_3N$: N, 6.57; found: 6.57.

0.2518 gram took 11.83 cc. 0.1 *N* NaOH; calculated, 11.81 cc.

---

[1] Walden, *Ber.*, **29**, 138 (1896).

[2] Secondary refers to the position of the carboxyl group.

[3] *Am. Chem. J.*, **24**, 503 (1894).

[4] *Ibid.*, **24**, 507.

Decomposition of the Nitroso Derivative of Anhydroaminocampholytic Acid.—Ten grams of the nitroso compound were mixed with 50 cc. of a solution of sodium hydroxide (5%) and the mixture distilled with steam. The products obtained from four lots treated in this manner were united and separated as follows: The isolaurolene (C_8H_{14} boiling at 106–110°) was separated from the aqueous distillate. To the alkalin solution somewhat less than enough sulfuric acid to combine with the sodium present was added and the campholytic acid and campholytolactone distilled over with steam. The *trans*-hydroxydihydrocampholytic acid was obtained from the residue in the distilling flask. The campholytic acid and lactone were extracted with ether and separated by solution of the campholytic acid in a solution of sodium or potassium carbonate and extraction of the lactone with ether. The nitroso compound gave approximately the following percentages of its weight:

Isolaurolene	3%
Campholytolactone	4%
Campholytic acid	7%
Trans-hydroxydihydrocampholytic acid	45%

Direct Decomposition of Aminodihydrocampholytic Acid with Nitrous Acid.—The most satisfactory conditions which have been found for the direct decomposition of aminodihydrocampholytic acid are the following: Fifty-seven grams of the amino acid are dissolved in 200 cc. of water and 18 cc. of dilute sulfuric acid (1 : 1) and to the solution 30 grams of solid sodium nitrite are added. After the first rapid decomposition is over a little more acid may be added and after an hour or two the decomposition products may be taken up with ether and separated as already described. If it is desired to recover the isolaurolene, the solution must be neutralized and distilled with steam before the addition of the ether. The products are approximately the following percentages of the weight of the amino acid:

Isolaurolene	0.7%
Campholytolactone	5.3%
Campholytic acid	2.0%
Trans-hydroxydihydrocampholytic acid	45.0%

About 30% of the amino acid escapes decomposition and a part of this may be recovered. It is noticeable that much less isolaurolene is formed by the direct decomposition of the amino acid than by the decomposition of the nitroso derivative of the anhydride. This corresponds with the conduct of aminocamphonanic acid.[1]

The most remarkable fact of the decomposition is that the hydroxydihydrocampholytic acid, which forms the principal product, has the hydroxyl and methyl groups on opposit sides from the amino and methyl

---

[1] THIS JOURNAL, 31, 671 (1909).

groups of the original compound, while the campholytolactone which is formed in relatively small amounts retains the original configuration. As has been pointed out, this is due to a Walden inversion, which is not, however, complete.

d-Trans-*hydroxydihydrocampholytic Acid* has been prepared by several different persons. When carefully purified by crystallization from ethyl acetate it melts at 133.7°. $[\alpha]_D = 70.1°$; 8 grams in 100 cc. of ethyl acetate. As has been stated by one of us, it may be distilled rapidly with only slight decomposition. Ten grams, when distilled very slowly, gave 2.8 grams of campholytic acid ($[\alpha]_D = -49.6°$), about 0.3 gram of campholytolactone and a considerable amount of unchanged *trans*-hydroxydihydrocampholytic acid. The lactone of the *trans* acid *was not found among the products.* The campholytolactone was identified by conversion into *cis*-hydroxydihydrocampholytic acid.

Three grams of *trans*-hydroxydihydrocampholytic acid and 30 cc. of water were sealed in a tube and heated for 48 hours in a water bath. The tube opened with some pressure and the presence of carbon dioxide was demonstrated. Isolaurolene was identified by its boiling point (109–110°) and the other products as usual. These formed the following percentages of the weight of the hydroxy acid:

Isolaurolene	12%
Campholytolactone	7%
Campholytic acid	35%
Trans-hydroxydihydrocampholytic acid	35%

Here again the lactone of hydroxydihydrocampholytic acid *was not found.*

Lactone of Trans-*hydroxydihydrocampholytic Acid.*—As stated above, we have not been able to obtain this lactone by heating the acid either by itself at high temperatures or with water. Warming or even standing over night with dilute sulfuric acid (1 : 1) changes it to isocampholytic acid.[1] Even heating with acetic anhydride for a moment leaves it almost wholly unchanged.[2]

Bredt[3] has shown, however, that it may be converted into a lactone by warming for some time with acetic anhydride. We have confirmed this. Fifteen grams of hydroxydihydrocampholytic acid were put in a flask with 13.5 grams of acetic anhydride and the mixture heated on the water bath for an hour and a half. The acetic acid and anhydride were distilled under 20 mm. pressure, the residue dissolved in ether and the solution washed with a sodium carbonate solution and finally with a 5% solution

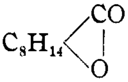
---

[1] *Am. Chem. J.*, **17**, 426 (1895).

[2] *Ibid.*, 26, 284 (1901).

[3] Inaugural dissertation of Jos. Pfeil (1901) from the laboratory of Professor Bredt. See also *Ann.*, **314**, 392 (1900).

of sodium hydroxide. After drying the ethereal solution, the lactone was precipitated with petroleum ether, in which it is much less soluble than is campholytolactone. Specific rotation, $[\alpha]_D = 121.9°$. One gram in 10 cc. of absolute alcohol solution at 27°. Two molecular weight determinations by the freezing point method with acetic acid as the solvent gave 175 and 180. Calculated for



$C_8H_{14}\langle{}^{CO}_{O}$, 154. It melts at 115–117°.

The melting point is so close to that of campholytolactone that Bredt has supposed that the two substances are identical. When the two are mixed, however, the melting point falls to 104–107°. Also the lactone gives on hydrolysis with sodium hydroxide the same *trans*-hydroxydihydrocampholytic acid from which it was formed,[1] while campholytolactone gives *cis*-hydroxydihydrocampholytic acid by the same treatment.

The conductivity of the hydroxy acid is given below.

Campholytolactone.—This was first prepared by Tiemann and Kerschbaum.[2] It is best crystallized from petroleum ether by cooling the solution with ice or a freezing mixture, as the solubility is much less at low temperatures. The highest melting point which we have found is 118–119°. A small amount of other substances lowers the melting point considerably and complete purification is difficult because of the waxy nature of the compound. The specific rotation, $[\alpha]_D = 8.5°$; 1.2 grams in 10 cc. of absolute alcohol. On warming with dilute sulfuric acid (1 : 1) campholytolactone is converted to isocampholytic acid.[3]

Cis-*hydroxydihydrocampholytic acid* has been described by Tiemann and Kerschbaum[1] as the "hydroxy acid corresponding to campholytolactone." It is much more easily soluble in ether than the *trans* acid and is most easily purified by dissolving in ether and precipitating with petroleum ether. After repeating this four times the acid melted sharply at 118.5°. Crystallization from ethyl acetate did not change the melting point. Tiemann[4] gives the melting point as 121°. The specific rotation, $[\alpha]_D = 50.8°$; 0.82 gram in 10 cc. of absolute alcohol.

The conductivity of the two hydroxy acids at 25° is as follows:

Trans-HYDROXYDIHYDROCAMPHOLYTIC ACID.	k.
0.01330 normal	8.1×10^{-6}
0.00665 normal	7.9×10^{-6}
0.00332 normal	8.1×10^{-6}
Mean	8.1×10^{-6}

Cis-HYDROXYDIHYDROCAMPHOLYTIC ACID.	k.
0.01221 normal	36.2×10^{-6}
0.00610 normal	35.8×10^{-6}
0.00305 normal	35.5×10^{-6}
	35.8×10^{-6}

---

[1] *Loc. cit.*

[2] *Ber.*, **33**, 2938.

[3] *Ibid.*, **33**, 2938.

[4] *Ibid.*, **33**, 2938.

The greater conductivity of the *cis* form is of considerable interest in connection with a hypothesis recently proposed by one of us[1] connecting the ionization of acids with the electron theory. Whether that hypothesis is true or not, it seems pretty clear that in these acids the hydroxyl groups exert a greater or less effect on the ionization of the carboxyl according as the two are nearer together or further apart in space and in addition to any effect through the atoms connecting them.

One gram of the *cis* acid was heated in a sealed tube with 10 cc. of water in a water bath for 48 hours as described above for *trans*-hydroxydihydrocampholytic acid. The tube opened without pressure and there was no odor of isolaurolene. About 0.3 gram of campholytolactone melting 116–117° was obtained from the contents of the tube. It was identified by hydrolysis to *cis*-hydroxydihydrocampholytic acid. On heating by itself for 15 minutes at 225° the *cis* acid is partly converted into campholytolactone. The difference between the two hydroxy acids both on heating with water and on direct heating is very marked and evidently significant.

Attempts to Oxidize the Hydroxy Acids to Ketonic Acids.—Half a gram of *trans*-hydroxydihydrocampholytic acid was mixed with twice the theoretical amount (3 cc.) of Beckmann's chromic acid mixture[2] and the mixture allowed to stand over night, 2 cc. of dilute sulfuric acid (1 : 1) were then added and the mixture allowed to stand for 24 hours longer. The mixture darkened somewhat, but did not turn green and the hydroxy acid was recovered mostly unchanged. An exactly similar experiment with the *cis* acid gave the same result. As camphonolic acid is easily oxidized to camphononic acid by this treatment and as neither acid was converted to a lactone by the action of the acid, it seems to be very certain that the hydroxyl group is tertiary in each acid. As each acid has been reduced to the same dihydrocampholytic acid (see below) through the iodo acid, any other explanation of the isomerism of the two acids than that they are *cis* and *trans* stereomers seems to be excluded.

In a conversation with Professor Bredt he has pointed out that the lactone of *trans*-hydroxydihydrocampholytic acid is, as far as we know, the first *trans* lactone of a cyclic compound which has been found. It is difficult to reconcile its existence with the ordinary view of the stereomeric forms of the two hydroxy acids, but we are unable to give any other interpretation of the relations which have been found. Tiemann[3] suggested that the hydroxydihydrocampholytic acid and the hydroxy acid from the campholytolactone might be *cis-trans* isomers but a *cis-trans* isomerism of the lactones is considered here for the first time.

---

[1] THIS JOURNAL, **34**, 663 (1912).

[2] *Ann.*, 250, 325.

[3] *Ber.* **33**, 2939 (1900).

Campholytic Acid.—Walker, who first prepared this acid[1] by the electrolysis of the acid ester of camphoric acid obtained an acid with only a slight optical activity. Some years later the acid obtained by the decomposition of aminodihydrocampholytic acid[2] was found to have a rotation of —59.6° at 18°. When it was found that *trans*-hydroxydihydrocampholytic acid is converted in part to campholytolactone by heating with water it was concluded that the methods of purification used before must have given an acid containing some campholytolactone. By distilling twice more with steam to secure a more complete separation from the hydroxy acid and by dissolving in a solution of potassium carbonate and extracting the lactone with ether, an acid with a rotation $[\alpha]_D =$ —70.0° at 29° has been obtained. By decomposing the iododihydrocampholytic acid from *cis*-hydroxydihydrocampholytic acid with sodium bicarbonate, an acid for which $[\alpha]_D =$ —74.3° at 30° (0.2 gram in 10 cc. petroleum ether) was prepared. It seems probable that the various preparations contained some of the racemic form and that the pure, active acid may have a higher rotation than any of the values given. It is possible, also, that all of the samples contained some isocampholytic acid, from which it would be difficult or impossible to separate it.

We have not found any evidence that campholytic acid is changed to campholytolactone by heating it with water. Heating or standing with dilute acids converts it into isocampholytic acid, in which a methyl group has shifted from the β- to the γ-position.[3]

The conductivity of *l*-campholytic acid and of isocampholytic acid we have found as follows at 25°:

l-CAMPHOLYTIC ACID.	*k*.
0.00649 normal..........	9.98×10^{-6}
0.00324 normal..........	9.75×10^{-6}
0.00162 normal..........	9.71×10^{-6}
Mean..............	9.8×10^{-6}

ISOCAMPHOLYTIC ACID.	*k*.
0.00116 normal......	8.1×10^{-6}
0.00058 normal......	7.95×10^{-6}
(0.00029 normal......	10.6×10^{-6})
	8.0×10^{-6}

The last value for isocampholytic acid, which was obtained with a very dilute solution, is omitted from the mean. The results agree with the common experience that a Δ^1 unsaturated acid has a lower conductivity than a Δ^3 acid. Walker's values[4] for the two acids, recalculated to the same unit, are for campholytic acid (nearly inactive) 8.0×10^{-6}, for isocampholytic acid, 7.4×10^{-6}.

d-*Iododihydrocampholytic acid* was prepared in three different ways:

I. Ten grams of *l*-campholytic acid were placed in a U-tube with 25 cc.

---

[1] *J. Chem. Soc.*, **63**, 498 (1893); **77**, 377 (1900).

[2] *Am. Chem. J.*, **24**, 290 (1900).

[3] THIS JOURNAL, **34**, 176 (1912).

[4] *J. Chem. Soc.*, **77**, 399 (1900).

of low boiling petroleum ether and hydriodic acid gas was passed through the tube as long as crystals of the iodo compound separated. The petroleum ether was evaporated in a current of dry air. For analysis and the determination of optical rotation a portion of the compound was dissolved in carbon disulfide, some petroleum ether was added and the solution evaporated by continuous evacuation in a desiccator. The nearly white crystals were pressed on porous porcelain and weighed as soon as possible for analysis and determination of the rotation.

II. *Trans*-hydroxydihydrocampholytic acid was suspended in carbon disulfide, in which it is nearly insoluble. Hydriodic acid gas was passed into the mixture till the hydroxy acid was decomposed and the iodo-compound, which is easily soluble in carbon disulfide, had passed into solution. After removing the water formed with anhydrous sodium sulfate and evaporating the carbon disulfide in a current of dry air, the residue was treated as before.

III. From *cis*-hydroxydihydrocampholytic acid by exactly the same method used for the *trans* acid.

Owing to the fact that the iodo compound is extremely unstable and has no definit point for melting or decomposition and also because it can not be recrystallized without considerable decomposition, it can not be decided positively whether the same compound is formed by each method of preparation or whether the compound was in each case a mixture of the *cis* and *trans* forms. Each of the three gave by treatment with sodium bicarbonate, campholytic acid, *trans*-hydroxydihydrocampholytic acid and campholytolactone. Each gave dihydrocampholytic acid by reduction, differing somewhat in rotatory power, it is true, but each sample of the dihydrocampholytic acid gave the same crystallin amide, practically identical in rotatory power. The fact that the greatest difference in rotatory power of the three preparations of the iodo acid is only 6.5° while the difference between the *cis* and *trans* forms of the hydroxy acids is 19.7°, points rather strongly to the conclusion that the three preparations are essentially identical. In any case, *for each compound* a rearrangement must occur from the *cis* to the *trans* form or *vice versa* either in its formation or in its decomposition by sodium bicarbonate.

Here, again, we have a rearrangement which differs from the Walden, if at all, only in that it is incomplete. *The rational view seems to be that the Walden inversion is merely a limiting case of ordinary rearrangements, where the inter-atomic forces are such that the equilibrium in the formation of two possible forms lies far on the side toward the formation of one of these.*

The results obtained with the iodo compounds are as follows:

	I. From *l*-campholytic acid.	II. From *d*-*trans*-hydroxydihydrocampholytic acid.	III. From *d*-*cis*-hydroxydihydrocampholytic acid.
Iodine calculated for $C_8H_{14}ICO_2H$	45.02	45.02	45.02
Iodine found	44.54	44.15	44.34
$[\alpha]_D$ for *d*-iododihydrocampholytic acid	+99.4° at 28°, 0.42 g. in 10 cc. CS_2	+97.8° at 28°, 0.32 g. in 10 cc. CS_2	+92.9° at 23°, 0.29 g. in 10 cc. CS_2
$[\alpha]_D$ for *d*-dihydrocampholytic acid	34.6° at 25° (pure substance)	32.8° at 28° (pure substance)	36.5° at 22°, 0.7 g. in 10 cc. petroleum ether
$[\alpha]_D$ for amide of dihydrocampholytic acid in petroleum ether	20.7° at 21°, 0.11 g. in 10 cc.	20.3° at 22°, 0.82 g. in 10 cc.	21.2° at 24°, 0.11 g. in 10 cc.
Melting point of amide	86–86.5°	86–86.5°	85.5–86°
Melting point of mixed amides	86–86.5°	85.5–86.5°	
Products obtained by decomposing the three iodo compounds with a solution of sodium bicarbonate			
$[\alpha]_D$ for *l*-campholytic acid in petroleum ether	—61.4° at 28°, 0.52 g. in 10 cc.	—62.1° at 27°, 0.48 g. in 10 cc.	—74.2° at 21°, 0.21 g. in 10 cc.
Melting point of *d*-*trans*-hydroxydihydrocampholytic acid	131°	130°	129–131°
Melting point of mixture of hydroxy acids with *d*-*trans*-hydroxydihydrocampholytic acid	132°	132°	130–132°
Melting point of hydroxy acid from hydrolysis of the lactone	118–119°	118–119°	116–118°
Melting point of hydroxy acid from lactone mixed with *cis*-hydroxydihydrocampholytic acid	118–119°	118–119°	116–118°

The lactone was identified by conversion into *cis*-hydroxydihydrocampholytic acid because the lactone itself is waxy and difficult to purify, while the *cis* acid can be easily separated and identified.

d-*Dihydrocampholytic Acid*, $C_8H_{15}CO_2H$.—If the structures which have been considered are correct, the replacement of the hydroxyl groups of *d*-*trans*-hydroxydihydrocampholytic acid and of the *cis* acid by hydrogen and also the reduction of *l*-campholytic acid should all give the same dihydrocampholytic acid, since the latter contains only one asymmetric carbon atom. As already indicated above, the experiment has confirmed this conclusion. The reduction was carried out in the same manner as the reduction of *dl*-campholytic acid.[1] The iododihydrocampholytic acid was dissolved in alcohol and considerably more than the theoretical amount of zinc dust was added. After a short time some

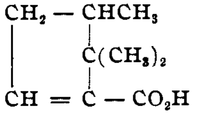
[1] *Am. Chem. J.*, **26**, 288 (1901); **27**, 426 (1902).

dilute sulfuric acid was added and then, after half an hour, or longer, the solution was diluted with water and the acids extracted with petroleum ether. After distilling the latter, the acids were dissolved in a 10% solution of sodium carbonate, the solution cooled with ice water and a 4% solution of potassium permanganate added in portions to destroy the unreduced campholytic acid. Sulfuric acid and acid sodium sulfite were added till the oxides of manganese passed into solution and the acids were extracted with ether and distilled with steam. The treatment with potassium permanganate was repeated to make sure of the removal of all unchanged campholytic acid and the purified acid was also dissolved in a solution of sodium carbonate and the solution extracted with ether to remove some campholytolactone which was likely to be present. The specific rotation of the acid and the melting point and rotation of its amide are given above. The acid is an oily liquid which has a specific gravity of 0.9915 at 20°.

Calculated for $C_8H_{15}CO_2H$: C, 69.11; H, 10.33.
Found: C, 69.21; H, 10.15.
0.0517 gram took 3.32 cc. 0.1 *N* NaOH; calculated 3.33 cc.

The *amide*, $C_8H_{15}CONH_2$, crystallizes from petroleum ether in plates, which melt at 86.5°.

Calculated for $C_9H_{17}ON$: N, 9.05%; found: 9.10%.

Attempt to Prepare Active Δ^5-Campholytic Acid.—The *dl*-Δ^5-campholytic acid, , was prepared some time ago.[1] It was hoped that by preparing the acid from *d*-dihydrocampholytic acid an optically active form could be obtained. The preparation was carried out essentially as with the racemic compound. The acid obtained melted at 91° and when mixed with some of the acid previously prepared the melting point was not changed. No rotation could be established for the acid with a 7% solution in alcohol. The preparation of the α-bromo derivative had evidently changed the original acid to a racemic form.

The solubility of Δ^5-campholytic acid is approximately one part in 5000 parts of water at 25°.

URBANA, ILLINOIS.

THE PHTHALYL CYANIDES.

BY GIBBS BLACKSTOCK.

Received June 4, 1912.

Some time ago Mr. C. H. Robinson, in this laboratory, prepared phthalyl cyanide in the hope of obtaining from it, by hydrolysis, the corresponding dibasic acid, but his work was interrupted before completion. The

---

[1] *Am. Chem. J.*, 26, 289 (1901).