[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

DEAMINIZATION OF METHYL DEXTRO-CIS-3-AMINO-1,2,2-TRIMETHYL CYCLOPENTANOATE

BY GLENN S. SKINNER

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Aliphatic diazo compounds have long been known to give by decomposition with dilute hydrochloric acid any or all of the following types of compounds: (1) alcohols, (2) unsaturated compounds, (3) chlorine derivatives, and (4) condensation products such as pyrazoline compounds. Recently, as a fifth type of reaction, the direct formation of the methyl ether of an hydroxy acid has been noted in the deaminization of the corresponding ester of an amino acid.[1] Very little quantitative study appears to have been made of the types of products formed in the deaminization of esters of amino acids, and our knowledge on this subject is largely based on the studies of the esters of diazo-acetic acid first undertaken by Curtius[2] and his students. It has, therefore, seemed advisable to study the diazo reaction from the standpoint of the products formed. In this investigation a quantitative examination has been made of the products of deaminization of the methyl ester of *d*-cis-3-amino-1,2,2-trimethyl-cyclopentanoic acid.

It has been noted that the products of decomposition of the above compound and those of its *trans* isomer differ considerably, the most striking difference being the non-formation of the ether from the *cis* compound. Since the decomposition has been carried out on a large scale this statement is considered to be accurate. The percentages of products obtained are as follows: *cis* compound, unsaturated esters, 62; hydroxy esters, 36; chloro esters, 2; methoxy acid, none; *trans* compound, 41, 46, undetermined, and 13, respectively.

The hydrochloride of the ester of the *cis* amino acid was diazotized in the usual way with the addition from time to time of a few drops of hydrochloric acid, such as was necessary to maintain the evolution of nitrogen until the reaction was complete. The products of the decomposition were extracted with sodium bicarbonate solution in order to remove any acid that might be present, and were then fractionally distilled under a pressure of 3–8 mm. A very efficient fractionating column should be used. The material was thus divided into 10 fractions boiling over a range of 56° (5.5 mm.) for the unsaturated ester to 109° (4 mm.) for the ester of the hydroxy acid having the highest melting point. The separation of 1 intermediate hydroxy ester (b. p.$_{3\,\text{mm.}}$, 88–89°) was quite sharp, but the boiling point of the other (b. p.$_{4\,\text{mm.}}$, 100–105°) was too near that of the higher- and lower-boiling compounds to allow complete separation with the amount of

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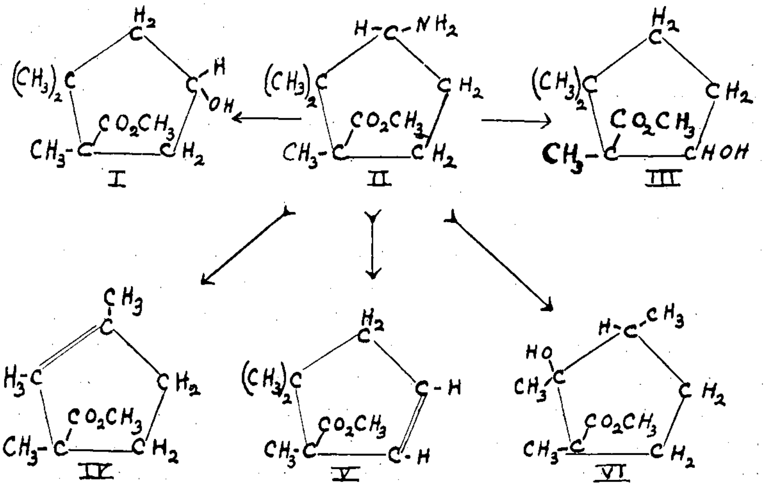
[1] Noyes and Skinner, THIS JOURNAL, **39**, 2692 (1917).

[2] Curtius, *Ber.*, **16**, 2230 (1883).

material at hand. Each of these fractions was then saponified by treatment with sodium alcoholate. All of the free acids were then distilled under diminished pressure with the exception of the acid from the highest-boiling fraction, which was isolated as the calcium salt. There was thus found to be present in the unsaturated-ester fraction the esters of 2 unsaturated acids, and in the hydroxy-ester fraction the esters of 3 hydroxy acids. Evidence has been obtained to show that the relationship which exists among these compounds is as follows.

Esters of Unsaturated Acids

The entire amount of unsaturated compounds boiled over a temperature range of 5° and from this a constant-boiling fraction was separated for examination. The acid obtained by saponification proved to be largely lauronolic acid. It contained no Δ_3 acid and only a comparatively small amount of the Δ_2 acid which was also found to be present in the lauronolic acid obtained from the ester of the *trans* amino acid. The pure lauronolic acid gives a bromolactone melting at 194° and the Δ_2 acid a dibromo acid melting at 189°. The Δ_3 acid has a specific rotation of approximately +40° and its presence in lauronolic acid may be detected either by the formation of the dibromo acid or by oxidation with permanganate. The



I, Methyl *l-trans*-3-hydroxy-1, 5, 5-trimethyl cyclopentanoate.

II, Methyl *d-cis*-3-*amino*-1, 2, 2-trimethyl cyclopentanoate.

III, Methyl *d*-2-*cis*-hydroxy-1, 5, 5-trimethyl cyclopentanoate.

IV, *d*-lauronolic acid methyl ester.

V, Methyl ester of the Δ_2 acid.

VI, Methyl *d-cis*-2-hydroxy-1, 2, 3,-trimethyl cyclopentanoate.

Fig. 1.

yield of the oxidation product is very poor and the amount of the Δ_2 acid present is believed to be more accurately determined by the amount of dibromo acid obtained from the mixture. When thus determined the amount indicated is still not quite sufficient to account for the low rotation of the acid obtained through the nitrite decomposition, showing that some racemization has taken place.

Tiemann[3] states that the lauronolic acids from camphanic acid and also from the amino acid give a high- and a low-melting bromolactone. The low-melting bromolactone is also obtained by dissolving the above mentioned pure dibromo acid in sodium carbonate solution. Lauronolic acid was, therefore, prepared from *d*-bromocamphoric anhydride and from camphanic acid. The high-rotating acid (α_D, 197°) from *d*-bromocamphoric anhydride gave none of the second lactone (m. p., 94°), the acid (α_D, 147°) gave a moderate amount, while the acid (α_D, 97°) from the nitrite decomposition gave a much greater yield. Upon treatment with sodium alcoholate the high-melting lactone, which is formed directly, gives a dihydroxy acid which may be separated from its lactone by precipitation from ether solution with petroleum ether, but which on standing in contact with the mother liquor is transformed to the lactone. On the contrary, the bromolactone from the most stable intermediate dibromo acid by the same treatment gives at once the lactone of a dihydroxy acid. Hence, it is evident that the ease of lactone formation in the hydroxy compounds is the reverse of that in the case of the bromine derivatives. This, together with the fact that the hydroxy lactones are different and both inactive, argues that they are not derived from the *d* and *l* forms of the same unsaturated acid. Moreover, ring formation in the dextro compounds with the *cis* configuration in this series of cyclopentane derivatives very markedly decreases the positive rotation. Conversely, lactone formation in the *levo* series should increase the positive rotation, but it has been found that the bromolactone with the negative rotation comes from a dibromo acid having a positive rotation. One is thus led to the conclusion that both bromolactones have the *cis* configuration, being derived from lauronolic acid and the Δ_2 acid, respectively. This interpretation will be best understood by an examination of the following reactions.

Esters of Hydroxy Acids

Four crystalline acids have been isolated, but of one melting at 132–133° less than 0.1 g. was obtained, so that it could not be characterized. Only one of the acids was identical with an hydroxy acid obtained from the ester of the *trans* acid, namely, *d*-2-*cis*-hydroxy-1,2,3-trimethyl-cyclopentanoic acid. *d*-*Cis*-camphonolic acid which would ordinarily be expected in this decomposition could not be isolated. The remaining two have not been pre-

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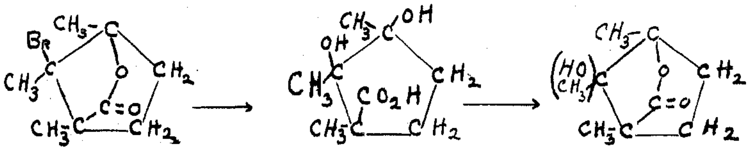
[3] Tiemann, *Ber.*, **33**, 2948 (1900).

viously isolated. The third acid has been shown to be *l-trans*-3-hydroxy-1,5,5-trimethyl-cyclopentanoic acid, the evidence being as follows. (a) It gives no camphononic acid upon oxidation with Beckmann's chromic acid mixture, and the liquid acid thus obtained upon further oxidation with permanganate gives camphoronic acid. This shows that the hydroxyl is on the γ carbon atom which is not adjacent to the *gem* methyl group. (b) The iodide of this acid gives upon decomposition with sodium carbonate solution an unsaturated acid and a small amount of an inactive lactone. The acid itself is *levo*rotatory but the unsaturated acid thus obtained is *dextro*-rotatory. It is not converted to a lactone by heat. These facts show that the hydroxyl is in the *trans* position.

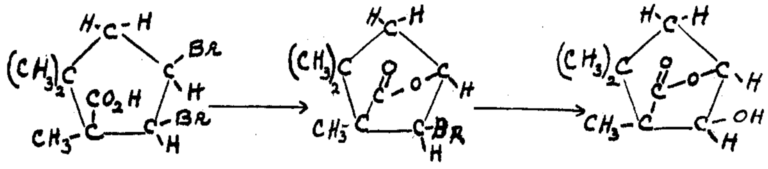
The evidence that the acid melting at 210° is *i*-2-hydroxy-1,5,5-trimethyl-cyclopentanoic acid is as follows. (a) When heated at a temperature of 255° it is not converted to a lactone, but sublimes unchanged. This indicates that the hydroxyl is not on either of the γ carbon atoms in the *cis* position. (b) Upon oxidation with Beckmann's chromic acid mixture it behaves exactly as *d-cis*-camphonolic acid, but the crystalline acid formed gives no camphoronic acid by further oxidation with permanganate. This indicates that the hydroxyl is secondary and also that it is not on either of the γ carbon atoms. It must, therefore, be in the β position in a compound in which the methyl groups substituted in the ring have not shifted.



From lauronolic acid.

M. p. = 194° M. p. = 174° M. p. = 215°

α_D = 51° α_D = 6° α_D = 0°



From the Δ_2 acid.

M. p. = 189° M. p. = 92° M. p. = 226°

α_D = 94° α_D = −65° α_D = 0°

Fig. 2.

These relationships will be clear from an examination of the structural formulas given above. The acid (m. p., 218°) resulting from the chromic acid treatment of the last mentioned hydroxy acid gave an acid which was not camphoronic acid but which was too small in amount for further study.

The unstable iodide from the new *levo* hydroxy acid upon decomposition with sodium carbonate solution gives a *dextro*rotatory unsaturated acid. Reasoning from its method of preparation and from the fact that it does not give camphoronic acid upon oxidation with permanganate, it must be the Δ_2 acid.

Suggestions as to the Course of the Reaction

It is still a matter of uncertainty as to whether the Curtius or the Angeli-Thiele formula more correctly represents the properties of aliphatic diazo compounds. The difficulty lies in the fact that their addition reactions as well as substitution reactions are subject to interpretation by either formula. Staudinger[4] has reviewed the properties of aliphatic diazo compounds in a consideration of the merits of the two formulas. Noyes and Chiles[5] have recently prepared some optically active diazo compounds from esters of amino acids. But even here it is possible to explain the optical activity by either formula, provided the two bonds of carbon to the diazo group are regarded as being different.

The methyl esters of the following amino acids should give with nitrous acid the ester of the same diazo acid whether formulated by the Curtius or the Angeli-Thiele method as they are ordinarily written according to the atomic linking theory.

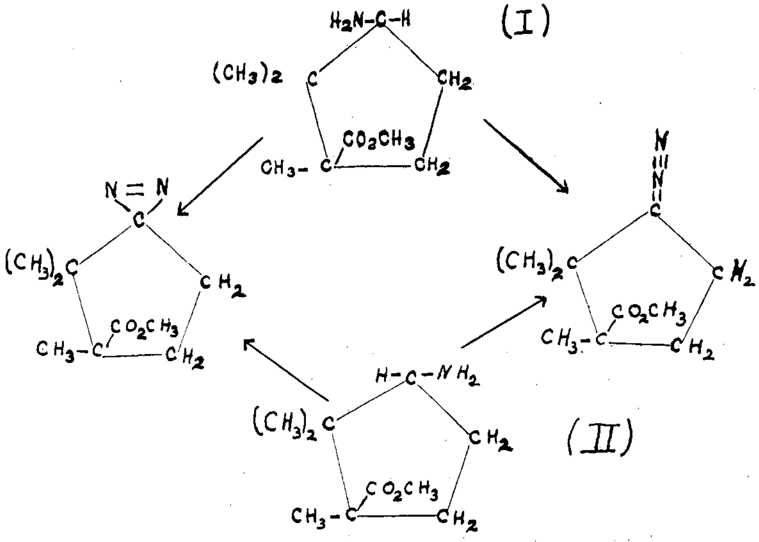


Fig. 3.

However, in the Curtius formula the diazo compounds derived from the *trans* (I) and the *cis* (II) have the nitrogen atom of the original amine on

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[4] Staudinger, *Ber.*, **49**, 1884 (1916); *Helvetica chim. Acta*, **4**, 239 (1921).

[5] Noyes and Chiles, THIS JOURNAL, **44**, 1798 (1922).

opposite sides of the ring and in the sense that the nitrogen atoms of each diazo compound are different the two diazo compounds are different. Similarly, in the Angeli-Thiele formulation of the 2 compounds there can be a difference only if the 2 bonds between the carbon and nitrogen atoms are different. These intermediate compounds must be different, since they give very different decomposition products.

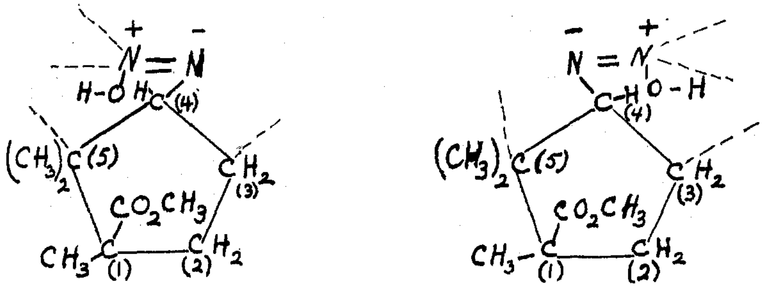
While at this stage of the investigation no theory to explain the reactions is warranted, nevertheless the facts can be coördinated by making use of certain assumptions which lead to the following pictures of the diazo compounds at the moment of decomposition.

1. The nitrogen atoms of the intermediate diazo compounds have the positive-negative character of the nitrogen atoms of the original amine and nitrous acid.

2. The positive-negative affinity of atoms or groups of atoms in these compounds is not satisfied solely as indicated by structural formulas, but by all of the atoms or groups of atoms within the molecule in varying amounts, and it is satisfied to a smaller extent by other molecules in the medium in which it is present.

3. The true diazo compound and the *syn* diazo hydrate are in reversible equilibrium through the addition and dissociation of water.

4. The affinities of the positive nitrogen and either of the carbon atoms in Position 3 with respect to this nitrogen atom are not completely satisfied, giving rise to partial valences mainly in the 1,4 positions.



Derivative of *cis* acid. Derivative of *trans* acid.

Fig. 4.

5. Addition may take place wherever these partial valences appear, as indicated by the dotted lines.

This scheme would explain the intimate connection between Positions 3 and 5 with respect to (4) which has been confirmed by experiment. It is, however, believed to be only one of the ways in which the reaction may take place. It will be noted that the hydroxyl of the diazo hydrate resulting from the *trans* compound is on the same side of the ring as the carboxymethyl group. This would more easily permit a metathesis between the hydrogen of this hydroxyl and the methyl radical of the carboxymethyl group. This compound by the loss of nitrogen would give the methyl ether of a free hydroxy acid. In order for the methoxy group to be in the *cis* position, a Walden inversion must take place. This possibility is precluded in the case of the diazohydrate from the ester of the *cis* amino acid since the hydroxyl group is then on the opposite side of the pentamethylene ring, which is in accord with the direction of the valences of the nitrogen atom as proposed by Hantsch and Werner.

Experimental Part

Hydrochloride of Methyl-*d*-*cis*-3-amino-1,2,2-trimethyl-cyclopentanoate.—*α*-*d*-Camphoramidic acid was prepared from *d*-camphoric anhydride by heating it with ammonium hydroxide in pressure bottles according to the method of Noyes[6] and Taveau. *α*-*d*-Camphoramidic acid (99.5 g.) is dissolved in 500 cc. of a 10% solution of sodium hydroxide. To this is added with stirring a sodium hypobromite solution prepared by treating 700 cc. of cold 10% sodium hydroxide solution with 80 g. of bromine. The solution is heated at a temperature of 75° for a half hour. The solution is cooled, sulfite is added, and the mixture is then poured with stirring into a large porcelain dish containing 200 cc. of hydrochloric acid (d., 1.19) diluted with an equal volume of water. If the solution is yellow more sulfite is added. Evaporation is continued to a volume of 450 cc. and the mixture allowed to cool. The hydrochloride should crystallize, and if the separation appears to be incomplete more acid should be added. The product is filtered with suction and freed from inorganic salts by recrystallization from water; yield, 85–90%. The dry hydrochloride of the acid (250 g.) is dissolved in 1 liter of dry methyl alcohol to which is slowly added 125 cc. of concd. sulfuric acid, and the mixture is refluxed for 48 hours on a steam-bath. The methyl alcohol is distilled rapidly under diminished pressure. The ester is liberated by the addition of crushed ice and sodium hydroxide, and then extracted with ether. The hydrochloride is precipitated from the solution, after drying with sodium sulfate, by hydrogen chloride. The yield is poor, amounting to 115 g. After drying at 110° the product gave the following data:

Analyses. Calc.: Cl, 16.00: Found: 16.11, 16.03. $[\alpha]_D$, 29.4° (0.05 g./cc. alcohol); $[\alpha]_D$, 29.2° (0.10 g./cc. alcohol); $[\alpha]_D$, 20.4° (0.04 g./cc. water); m. p., 237–238°.

Decomposition of the Hydrochloride.—To a solution of 100 g. of the hydrochloride in 400 cc. of water is added a solution of the equivalent amount of sodium nitrite in 100 cc. of water. After the mixture has been kept at room temperature for 84 hours, with occasional addition of a drop of hydrochloric acid when the reaction rate becomes small, the evolution of nitrogen will have practically ceased. The reaction proceeds more slowly than in the case of the *trans* isomer. The acid solution is then extracted with ether, the ethereal solution is dried with anhydrous sodium sulfate, and after distillation of the ether the residual esters are fractionally distilled 8 times under low pressure, using a long, efficient fractionating column.

The absence of free acids was determined by extracting the original ether solution with sodium bicarbonate solution. The yield was only about 80%, due partly to incomplete reaction and the formation of a small quantity of very high-boiling nitrogen-free condensation products. This contrasts with a yield of approximately 90% and formation of only traces of the very high-boiling material from the *trans* compound. Seven runs were made to prepare the material for fractional distillation.

Unsaturated Compounds.—More than 100 g. of the unsaturated ester was obtained

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[6] Noyes, *Am. Chem. J.*, **32**, 287 (1904).

of such purity that the entire amount distilled within a temperature range of 0.5°. Some of the boiling points observed are as follows: 85° (21 mm.); 75° (15 mm.); 72° (12 mm.); 65° (9 mm.); 56° (5.5 mm.); 51° (4 mm.). It was found during the course of the various fractionations that it is quite necessary to keep the pressure and the temperature of the Wood's metal bath as low as practicable to still insure complete condensation of the distillate. The ester thus obtained gave the following additional physical constants: d_4^{20}, 0.9649, d_4^{25}, 0.9607, $\alpha_D^{25°}$, 68.5°; $\alpha_D^{23°}$, 66.5°, for a solution in absolute alcohol containing 0.1037 g./cc.; n_{706}, 1.4484; n_{587}, 1.45267; n_{501}, 1.4580; n_{486}, 1.4590; n_{447}, 1.4631, at a temperature of 25°.

The ester (42 g.) is dissolved in 45 cc. of ethyl alcohol and to this is added 45 cc. of sodium hydroxide (3 cc. = 1 g.) The mixture soon becomes homogeneous and when refluxed in this way for 24 hours on a steam-bath the saponification is practically complete with very little darkening. After distillation of the alcohol under diminished pressure the unsaturated acid is liberated from the aqueous solution with hydrochloric acid and extracted with ether. After drying with anhydrous sodium sulfate and removing the ether the acid is distilled under diminished pressure using an efficient fractionating column. With the temperature of Wood's metal bath at 148° the acid distils constantly at 108° (4 mm.); yield, 34 g. It gave the following constants: $[\alpha]_D^{18.2°}$, 97.3°; $[\alpha]_D^{28.1°}$, 93.6°; $[\alpha]_D^{23°}$, 74.9°; $[\alpha]_D^{27.9°}$, 71.6° (0.0976 g./cc. in absolute alcohol.); n_{706}, 1.4569, n_{587}, 1.47056, n_{486}, 1.4775; n_{447}, 1.4811.

Oxidation of the Unsaturated Acid.—In order to determine the nature of the acid 5 g. was dissolved in the equivalent quantity of sodium hydroxide and diluted to 25 cc. A 1% solution of potassium permanganate was added to the cold solution with vigorous stirring until the color was only slowly discharged. No crystalline acid could be isolated at this stage of the oxidation, but when the reaction mixture was treated with successive small portions of dil. permanganate at room temperature until the color remained for about 10 hours it was possible to isolate 0.05 g. of a crystalline acid identical with 1,2,2-trimethyl-1-carboxy-glutaric acid.[7] In all of the runs that were carried out evidence of the absence of camphoronic acid was obtained at each stage of the oxidation by the non-precipitation of the barium salt from a boiling alkaline solution. When the alkaline solution from the first stage of the oxidation is distilled with steam a small amount of a volatile ketone is obtained. After an excess of permanganate is used it is still possible to obtain a considerable quantity of the unchanged acid as an insoluble oil in the distillate from acid solution, its identity being determined by analysis of the silver salt.

Analysis. Subs., 0.1500; Ag 0.0624. Calc. for $C_8H_{13}CO_2$: Ag, 41.4. Found: 41.6.

The silver salt of the volatile water-soluble acid darkened rapidly and was too unstable for analysis.

The Dibromo Acid.—To a solution of 10 g. of the acid in 30 cc. of chloroform cooled in ice water was added dropwise, with continuous shaking, 3.7 cc. of bromine. After all had been added the flask was allowed to stand in ice for 1 hour. After filtration with suction the weight of the almost white crystalline product was 5.5 g. Large transparent crystals (4 g.) were obtained from benzene, which melted sharply to a clear liquid at 189°. The analysis for bromine was carried out by the Carius method using 1.3 cc. of fuming nitric acid and heating at a temperature of 300–340° for 2 hours.

Analysis. Subs., 0.2922: AgBr, 0.3498. Calc. for $C_8H_{13}Br_2CO_2H$: Br, 50.91. Found: 50.95. $[\alpha]_D^{21°}$, 94.1°; $[\alpha]_D^{29°}$, 91.6° (0.0994 g./cc. of absolute alcohol).

The Bromolactone from the Dibromo Acid.—One g. of the dibromo acid was finely powdered in an agate mortar and treated with 10 cc. of a 5% solution of sodium carbonate. The material immediately dissolved but the solution became turbid in a few

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[7] Compare THIS JOURNAL, 39, 2703 (1917).

minutes with the separation of the crystalline bromolactone. The product melted at 91–92° (cor.) and after recrystallization from 16 cc. of hot 35% alcohol the product which separated in the form of white glistening scales melted at the same temperature. Tiemann gives 94° for this lactone. The rotation for a solution in absolute alcohol containing 0.04517 g./cc. was $[\alpha]_D$ —65°.

The High-melting Bromolactone.—In order to obtain the other lactone, the product obtained by the evaporation of the chloroform in a current of dry air at room temperature was rapidly triturated in a mortar with successive portions of dil. sodium carbonate solution and at once filtered. After standing on a porous plate in a closed vessel it was crystallized from hot ligroin; m. p., 188–189°. On further recrystallization[8] the melting point becomes 194°; $[\alpha]_L$, 51.0°.

The Hydroxy Lactone from the Low-melting Bromolactone.—The low-melting lactone (1.5 g.) when treated with warm sodium alcoholate, prepared from 0.5 g. of sodium and 7 cc. of 95% alcohol, reacts vigorously with the formation of the salt of a dihydroxy acid. An equal volume of water was added and the solution was distilled until most of the alcohol was removed, when it was filtered. The lactone of the dihydroxy acid was liberated with hydrochloric acid and found to melt at 224°. After recrystallization once from water the product weighed 0.7 g.; m. p., 225–226°. It crystallizes in the form of long needles which under the microscope were found to be 6-sided monoclinic prisms. It titrates at once to a sharp end-point with carbonate-free alkali.

Analysis. Subs., 0.1014: 11.75 cc. of 0.0506 *N* alkali. Calc. for C_9H_{14}: 11.77 cc. $[\alpha]_D$, 0 ± 0.01°.

Lauronolic acid was prepared by the method described by Aschan[9] and gave a rotation of $[\alpha]_D^{24°}$, 188°. However when the product thus obtained was redissolved in sodium carbonate solution which was then extracted with ether, the liberated acid gave a rotation of $[\alpha]_D^{19°}$, 197°. The highest rotation reported in the literature is that given by Tieman,[10] $[\alpha]_D^{19°}$, 199°. The acid boiled at 101–102° (2 mm.) with the Wood's metal bath at a temperature of 125–130°.

When 10 g. of the acid was treated with bromine in chloroform no dibromo acid separated. After distillation of the chloroform in a current of dry air the solid residue was triturated with sodium carbonate solution and filtered rapidly with suction. No bromolactone separated from the filtrate even on long standing. After one recrystallization from hot ligroin the residual high-melting lactone melted at 187–188°. When pure it melts at 194°.

Lauronolic acid prepared by dry distillation of camphanic acid gave the following constants: $[\alpha]_D^{19°}$, 147°; $\alpha_D^{23.5°}$, 117° (0.1 g./cc. of absolute alcohol); b. p.$_{13 \text{ mm.}}$, 108–110°. No dibromo acid separated upon treatment with bromine in chloroform solution. Ten g. of the acid yielded 1.1 g. of the low-melting lactone after trituration with sodium carbonate solution and rapid filtration. The high-melting lactone was shown to be identical with the corresponding lactone of acids obtained from the nitrite decomposition and from bromocamphoric anhydride.

The Hydroxy Lactone from the High-melting Bromolactone.—Several experiments were made on the saponification of the high-melting lactone according to the method used for the low-melting lactone. The product, a mixture of the lactone and dihydroxy acid, difficult to purify. From 8 g. of the bromolactone by repeated precipitation from concd. ether solution by petroleum ether a few tenths of a g. of the dihydroxy acid is described by Noyes and Skinner was obtained; m. p., 174–175°. When

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[8] Ref. 1, p. 2715.

[9] Aschan, *Ber.*, **27**, 3504 (1894).

[10] Ref. 3, p. 2946.

allowed to stand in contact with the mother liquor it changes into the lactone. A sample of the crude lactone, m. p., 205–14°, after recrystallization from hot water melted definitely at 214–215°. The observed rotation for a dilute solution in absolute alcohol was 0 ± 0.01°. When this substance was mixed with the lactone melting at 225–226° the melting point was indefinite at 180–205°. The substance crystallizes in long needles resembling those of the other lactone. In the titration the end-point was approached more slowly than in the case of the other lactone.

Analysis. Subs., 0.0506: 9.7 cc. of 0.0124 *N* alkali. Calc. for $C_9H_{14}O_3$: 9.76 cc.

The probable structures for these lactones are given in Fig. 2.

Esters of Hydroxy and Chloro Acids

Methyl *d-Cis*-2-Hydroxy-1,2,3-Trimethyl-Clyclopentanoate.—Twenty-seven and nine-tenths g. of the hydroxy ester, b. p.$_{2.5-3\ mm.}$, 88–89°, was saponified for 36 hours with an excess of sodium alcoholate. The free acid was fractionally distilled on account of the formation of some unsaturated acid from the chloro ester. The total amount of crystalline acid separating from the fraction boiling at 154° (6 mm.) or 145° (3.5 mm.) was 3.5 g. The liquid filtrate was converted to the calcium salt by use of calcium carbonate. The silver salt precipitated from a portion of the calcium salt was analyzed.

Analysis. Subs., 0.0800: Ag, 0.0310. Calc. for $C_8H_{14}(OH)COOAg$: Ag, 38.67. Found: 38.7.

The remainder of the solution upon concentration in a vacuum desiccator partially crystallized. From the crystalline portion was obtained an additional quantity of crude crystalline acid. After recrystallization from hot ligroin the total amount of pure acid melting at 102° was 3.5 g. The rotation for a solution in absolute alcohol containing 0.0569 g./cc. was $[\alpha]_D^{23°}$, 35.7°.

This fraction contained the largest percentage (6%) of esters of chloro acids. It was analyzed by the Carius method.

Analysis. Subs., 0.2422: AgCl, 0.0106. Calc. for $C_8H_{14}(Cl)CO_2CH_3$:Cl, 17.35. Found: 1.1.

Methyl-2-Hydroxy-1-5-5-Trimethyl-Cyclopentanoate.—The fraction boiling at 108–110° (4 mm.) gave the following constants: d_4^{20}, 1.0711; $[\alpha]_D^{23°}$, 29.9°; $[\alpha]_D^{22.8°}$, 29.6° (0.967 g./cc. of absolute alcohol).

It was saponified with sodium alcoholate for 26 hours. The dark colored, viscous acid was converted to the calcium salt which partly crystallized upon concentration of the aqueous solution. The free acid from the crystalline salt crystallized slowly from an ether solution after the evaporation of the ether and after crystallization from a mixture of benzene and ligroin the melting point was 209–210°; $[\alpha]_D$, 0 ± 0.01° (0.0206 g./cc. of absolute alcohol). The acid liberated from the sirupy filtrate from the crystalline salt crystallized after long standing. It was then allowed to remain upon a porous plate for several weeks and when recrystallized melted at 209–210°. When oxidized with Beckmann's chromic acid mixture according to the method used for the oxidation of *cis*-camphonolic acid it behaved in a similar manner. The dichromate began to darken almost immediately and the oxidation product was entirely crystalline. Recrystallized from hot benzene it melted at 218°. Upon oxidation of 0.1 g. of this acid with permanganate no trace of camphoronic acid was found as characterized by the properties of its barium salt. The amount of crystalline ketonic acid obtained was too small to identify. When heated at a temperature of 255° the hydroxy acid sublimed unchanged, being still completely soluble in sodium carbonate solution and melting at the same temperature as the original substance. Judging from the positive rotation of the ester and the large yield of the inactive acid obtained by saponification, the racemization must have taken place during the saponification rather than during the diazotization. This is in accord with the marked reactivity of β-hydroxy acids.

Methyl-l-*trans*-3-hydroxy-1,5,5-trimethyl-cyclopentanoate.—A fraction (21.5 g.) of the hydroxy esters, b. p.$_{5\text{ mm.}}$, 105–107°, gave a rotation of $[\alpha]_D^{23°}$, 22.4°. The hydroxy acid was obtained from this by saponification and fractionally distilled to separate it from the small amount of unsaturated acid formed by the action of the alkali on the ester of the chloro acid present. The acid boiled at 165° (5 mm.) and partly crystallized in the distilling bulb. After filtration with suction on a Hirsch funnel and allowing the residue to stand upon a porous plate, 2.5 g. of the crude crystalline acid was obtained. By repeated crystallization from a hot mixture of benzene and ligroin containing a comparatively small amount of benzene the pure acid was obtained in the form of silky tufts of fine needles; m. p., 121–22°; $[\alpha]_D^{27°}$, —10.3° (0.0329 g./cc. of absolute alcohol).

Analysis. Subs., 0.1031: 19.20 cc. of 0.03129 *N* alkali. Calc. for $C_8H_{14}(OH)CO_2H$: 19.14 cc.

When heated at a temperature of 255° for 20 minutes the material darkened considerably, but was still soluble in sodium bicarbonate solution, showing that it had not been converted to a lactone. The acid did not crystallize again. The acid (0.3 g.) was suspended in carbon disulfide and immediately dissolved when hydrogen iodide was passed in. The carbon disulfide was evaporated at room temperature in a current of dry air, leaving an unstable crystalline iodide. This when dissolved in dil. sodium hydroxide gave an unsaturated acid which in an absolute alcohol solution (0.0091 g./cc.) gave an observed rotation of 0.65 ± 0.10° in a 20cm. tube; $[\alpha]_D$, 35°. The experiment was performed in another way by adding ether when nearly all of the carbon disulfide had been evaporated and shaking with dil. sodium carbonate solution. The ether layer left upon evaporation a small amount of a straw-colored oil which crystallized upon standing. After standing on a porous plate covered with a watch glass, the crude lactone melted at 47–48°. The melting point is apparently lowered by isocampholactone. The observed rotation for a solution in alcohol containing 0.00125 g./cc. was 0.00–0.01°. The unsaturated acid which is apparently formed in slightly greater quantity gave by oxidation with dil. permanganate no trace of camphoronic acid. The oxidation product, to confirm further that it is the Δ_1 acid, has not yet been isolated for the lack of material. The hydroxy acid, upon treatment with chromic acid according to the method for the oxidation of *cis*-camphonolic acid, was oxidized similarly with the exception that the oxidation product remained as a viscous dark oil which after extraction with ether did not crystallize. The neutral solution after oxidation carried out by the addition of successive small portions of permanganate gave a strong reaction for camphoronic acid.

Summary

1. It has been shown that when the deaminization of methyl-*d-cis*-3 amino-1,2,2-trimethyl-cyclopentanoate is performed on a large scale no ether of a free hydroxy acid is formed. The products are formed in the following proportions: esters of unsaturated acids, 62%; esters of hydroxy acids, 36%; esters of chloro acids, 2%.

2. The unsaturated acids are lauronolic and the Δ_2 acid which retains the *gem* methyl grouping. Based upon the yield of the 2 bromolactones the 2 acids are present to the extent of approximately 70% and 30%, respectively.

3. The fractions of esters yielding hydroxy acids are present in approximately the following proportions: m. p., 102°, 65%; m. p., 121–122°, 20%; m. p., 210°, 15%.

4. Evidence is given that the acid melting at 121–122° is *l-trans*-3-hydroxy-1,5,5-trimethyl-cyclopentanoic acid.

5. Evidence is given that the acid melting at 210° is *i*-2-hydroxy-1,5,5-trimethyl-cyclopentanoic acid.

6. The lactones of the 2 dihydroxy acids derived from the unsaturated acids have been prepared and their properties studied.

7. The esters of the unsaturated and hydroxy acids undergo some racemization in their formation from the ester of the amino acid.

8. Some suggestions have been made which afford a partial explanation of the course of the reaction.

The study is being continued with a view to learning the mechanism of the diazo reaction in various types of compounds especially from the standpoint of the products formed. The properties of the diazo compounds themselves will be reported as soon as these compounds can be purified.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

THE BENZIL REARRANGEMENT. II

BY ARTHUR LACHMAN

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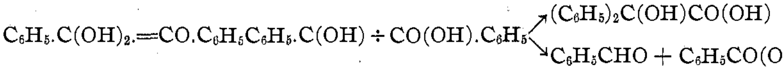
In a recent study[1] of the rearrangement of benzil to benzilic acid, it was pointed out that this reaction involves the process known as "intramolecular oxidation and reduction." It was also shown that this type of rearrangement, for which the much shorter term *metakliny* was suggested, is always accompanied, in varying degree, by a rupture of the molecule at the same point at which the metaklinic process is occurring.

It was possible to account for both reactions by the assumption of a shifting hydroxyl group. Benzil adds a molecule of water when it goes over into benzilic acid.

$$C_6H_5—CO—CO—C_6H_5 + H_2O = (C_6H_5)_2C(OH)CO.OH \qquad (1)$$

This addition must occur primarily at one of the carbonyl groups, and it is one of the hydroxyl groups thus formed which migrates.[2]



$$C_6H_5.C(OH)_2.{=}CO.C_6H_5C_6H_5.C(OH) \div CO(OH).C_6H_5 \begin{cases} \nearrow (C_6H_5)_2C(OH)CO(OH) & (2A) \\ \searrow C_6H_5CHO + C_6H_5CO(OH) & (2B) \end{cases}$$

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[1] Lachman, (a) THIS JOURNAL, **44**, 336 (1922). The literature of the benzil rearrangement given there need not be repeated here. An important omission, however, should be rectified. Jena, [(b) *Ann.*, **155**, 78 (1870)] heated 1 g. of benzil with water to 200° for 6 hours, and obtained 0.25 g. of benzilic acid, "very pure."

[2] For the use of the division sign, ÷, to indicate the *incomplete* shift, see Ref. 1a., p. 338. In that paper, the addition of *two* molecules of water to benzil was assumed, in order to make clearer the analogy between benzil and dihydroxy-tartaric acid. It seems more likely, from the data in the present paper, that only 1 molecule of water takes part in the reaction.