[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

MOLECULAR REARRANGEMENTS INVOLVING OPTICALLY ACTIVE RADICALS. XI. REARRANGEMENTS IN THE TRUXILLIC ACIDS AND THEIR BEARING UPON THEORIES OF MOLECULAR REARRANGEMENTS AND OPTICAL ROTATORY POWER

HERBERT I. BERNSTEIN[1] AND EVERETT S. WALLIS

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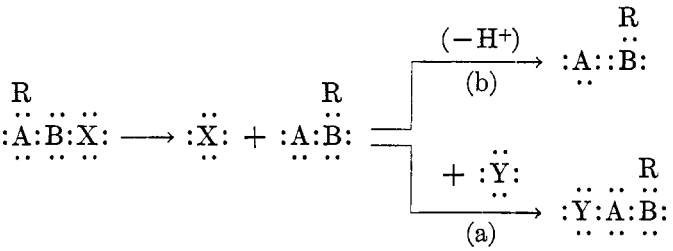
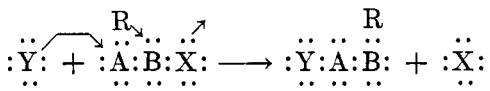
The modern electronic formulation for non-allylic molecular rearrangements as developed by Whitmore (1) may be illustrated by the following equation,

(I)



where A and B are atoms neither strongly electropositive nor electronegative, X and Y are strongly electronegative groups, and R is either an alkyl or aryl residue. The shifting of the group, R, follows simultaneously with the removal of $:\ddot{X}:$, R being apparently never completely free of either A or B (2). In rearrangements of the Wagner-Meerwein (retro-pinacolic) type, $:\ddot{Y}:$ may join the rearranged positive fragment (a), while in the pinacol rearrangement or in olefin formation, this fragment may lose a proton (b). It has also been pointed out (2 d, 3) that combination and rearrangement may be a single bimolecular process which can be formulated as follows,

(II)



analogous to substitution reactions of the S_N2 type (4), although at present there is no direct experimental evidence for this view.

Extensive studies in molecular rearrangements involving optically active groups have played an important role in the development and confirmation of the mechanism formulated in equation I. When R is an optically active group in which the asymmetric carbon atom is directly attached to A, it would be ex-

[1] National Research Fellow, Princeton University, 1940–41. Present address, Illinois Institute of Technology, Chicago, Ill.

pected on the basis of this mechanism to retain its complete activity. This has been shown to be true in earlier papers of this series (2 a, 5). Experimental studies have also shown that such a group not only retains its activity but also its configuration in conformity with an earlier suggestion in Part I (2 a) of this series. Thus, Noyes (6)[2] has shown in the *asymmetric* degradation of the camphoric acids that the rearrangement proceeds without inversion. A similar result has been obtained by Bartlett and Knox (8) in their studies of the Hofmann rearrangement involving hindered (bridge) systems, *i.e.*, the conversion of apocamphoric acid amide to the corresponding amine. A conclusive proof of this point for unhindered systems involving one asymmetric carbon atom is afforded in certain results (9) recently obtained in this laboratory on the Wolff rearrangement of optically active diazoketones.

For rearrangements of optically active molecules in which A is the asymmetric center, inversion or retention with more or less racemization would be expected from equation I, while inversion only should result from equation II. Experimental evidence is still somewhat confused. In certain studies (10) carried out in this laboratory of a retro-pinacolic type of rearrangement, partial racemization was observed. It should be noted, however, that this may have resulted from the unstable character of the tertiary chloride so produced. In considering the rearrangement of camphene hydrochloride to isobornyl chloride the results of kinetic studies are best explained by the bimolecular reaction of an intermediate positive camphene group and P Cl^- where P is a chloride carrier such as H^+ or a phenol (3, 11). Thus, $R:\underset{\cdot\cdot}{\overset{\cdot\cdot}{A}}:\underset{\cdot\cdot}{\overset{\cdot\cdot}{B}}:\underset{\cdot\cdot}{\overset{\cdot\cdot}{X}}: \rightleftarrows R:\underset{\cdot\cdot}{\overset{\cdot\cdot}{A}}:\underset{\cdot\cdot}{\overset{\cdot\cdot}{B}} + :\underset{\cdot\cdot}{\overset{\cdot\cdot}{X}}:$ is followed by the reaction

$$PCl^- + R:\underset{\cdot\cdot}{\overset{\cdot\cdot}{A}}:\underset{\cdot\cdot}{\overset{\cdot\cdot}{B}} \rightarrow P + :\underset{\cdot\cdot}{\overset{Cl}{\underset{\cdot\cdot}{\overset{\cdot\cdot}{A}}}}:\underset{\cdot\cdot}{\overset{\cdot\cdot}{\underset{R}{B}}}:$$

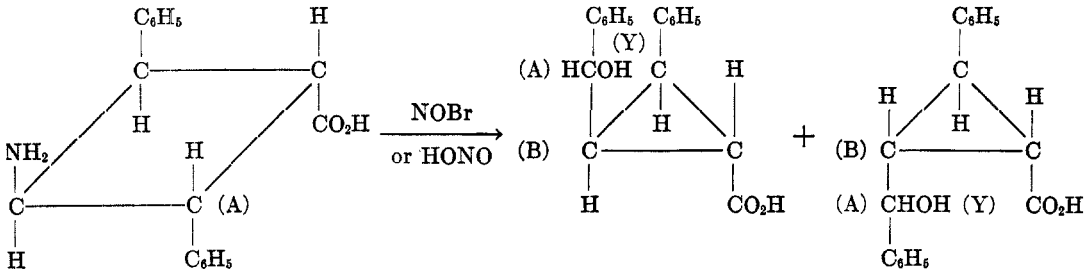
where the latter step, which is rate determining, is of the second order. It has been pointed out (3) that since bimolecular nucleophilic substitution reactions (4) occur with Walden inversion, inversion very probably occurs on the carbon atom holding the chlorine atom in isobornyl chloride.

The mechanism outlined above would also predict inversion of configuration involving carbon atom B. Kinetic studies (12) of the rearrangement of *cis*- and *trans*-7,8-diphenylacenaphthenediol-7,8 confirm this conclusion. Results of a similar nature were observed in kinetic studies (13) on the preparation of 2-indanone from both *cis*- and *trans*- indene glycol. Inversion of configuration has also been observed (14)[3] in the semipinacolic deamination of (−) 1,1-diphenyl-2-aminopropanol-1.

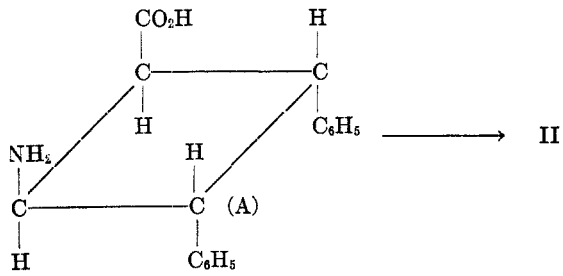
[2] Certain results of H. Fischer (7) obtained in the Curtius degradation of the amides of dihydroshikimic and quinic acids are of interest in this connection.

[3] In a recent paper by Kenyon and Young (*J. Chem. Soc.*, **1941**, 263), it is reported that (+) hydratropic azide is converted by the Curtius degradation into (−) α-phenylethylamine without appreciable racemization. We should like to point out at this time that this

In this paper we wish to present additional evidence for inversion at B. In part, this evidence has been obtained from a study of certain experimental researches of Stoermer and his co-workers (15) on the diazotization of the amino group in the truxillamic acids.[4] In an attempt to prepare certain hydroxyl derivatives of cyclobutane these investigators discovered that when the amino group in these acids was diazotized, a rearrangement occurred to give in each case various isomers of 1-carboxy-2-benzoxy-3-phenylcyclopropane, the configurations of which were determined. Thus,



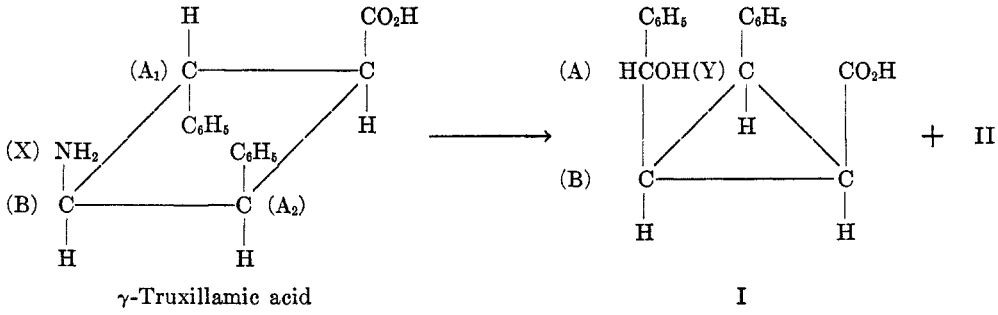
α-Truxillamic acid III II



β-Truxinamic acid

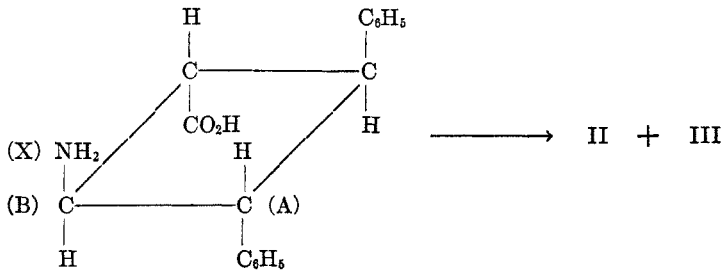
result is only a confirmation of the earlier work published from this laboratory in the first papers of this series. Moreover, for the particular molecule in question, the reaction was studied by Bernstein and Whitmore (14), reference to which was not made by Kenyon and Young. These investigators claim further to have submitted evidence to show that the course of the Beckmann transformation of optically active ketoximes is analogous to that of the Hofmann, Curtius, and Lossen rearrangements of related derivatives of optically active acids, a research project suggested by one of us in the title of Part I of this series. We find it regrettable that the investigation of Kenyon and Young has been conducted in so cursory a fashion as to permit no deductions concerning possible racemization during rearrangement. Indeed, it is not clear from these authors' experimental work whether optically pure starting materials were used, and granted that they were, no attempt was made to establish the degree of optical purity of the rearrangement product. We feel that the results of these authors must, therefore, be regarded as inconclusive and that a more precise investigation of the problem is necessary.

[4] These acids were prepared from the parent amido acid by the Hofmann degradation. In the light of our discussion on the asymmetric group, R, it is certain that the amino acids so produced are configurationally the same as the parent dibasic acids. The latter are well known. (See Rochussen and Niederländer in Richter's "Organic Chemistry", Nordemann Publishing Company, New York, **1939**, pp. 40–43.)

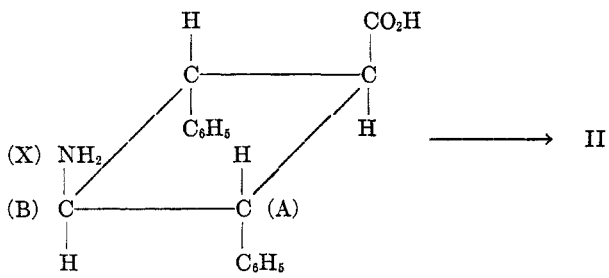


γ-Truxillamic acid

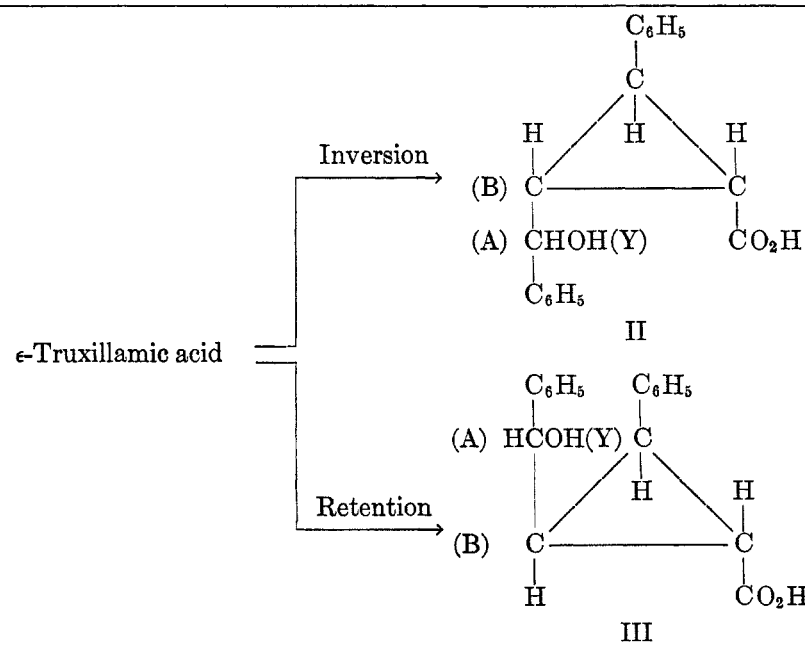
I



δ-Truxinamic acid



ϵ-Truxillamic acid



II

III

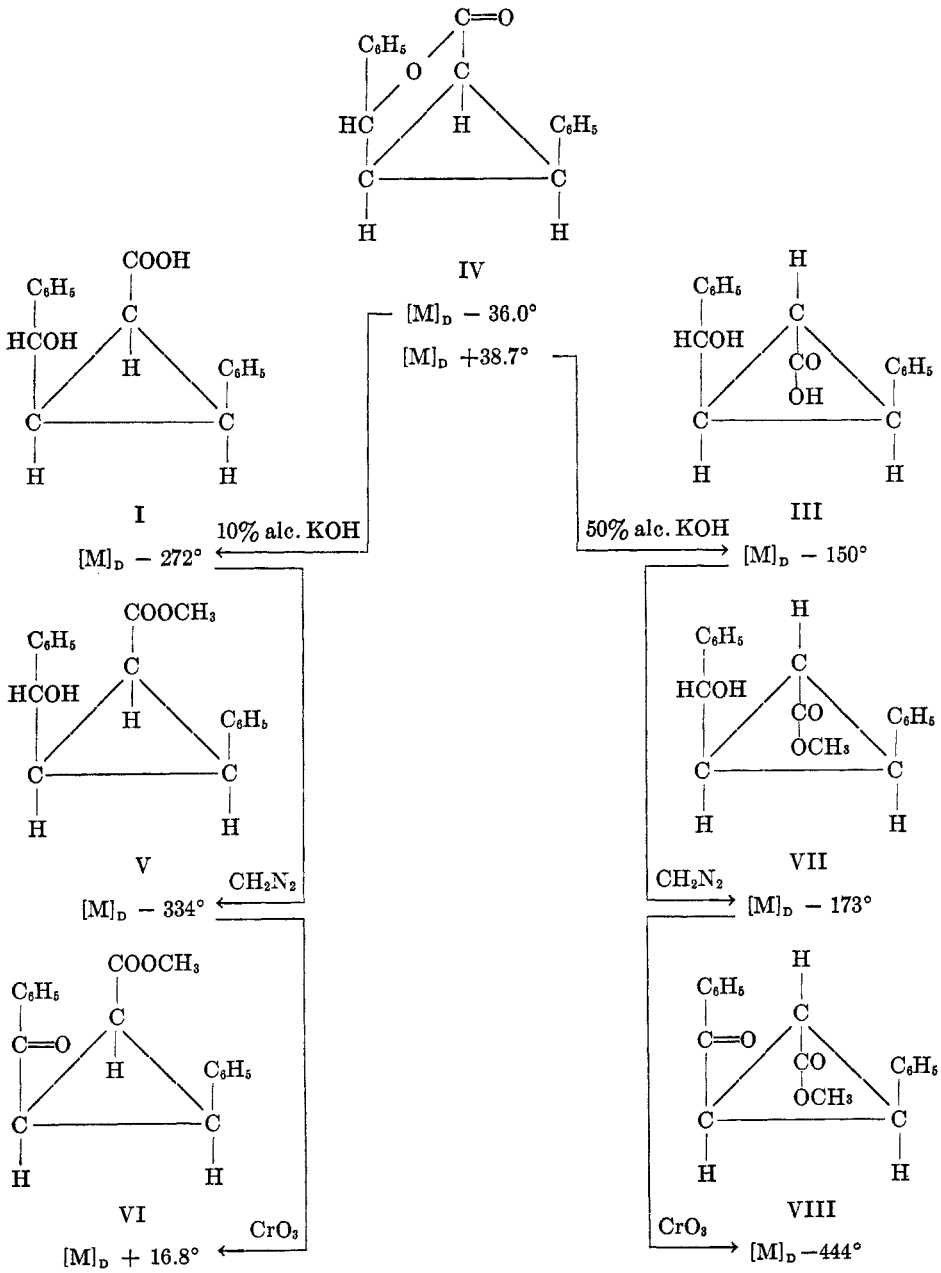
From a consideration of the spatial relationships involved, it can readily be seen that inversion or retention of configuration would lead to entirely different products. This is easily illustrated in the case of ϵ-truxillamic acid (see page 264.) Therefore, it is clear that with the β-, γ-, and ϵ-amino acids, all products of the rearrangement are the result of a rearward attack on the carbon atom holding the amino group. γ-Truxillamic acid yields both alcohols I and II because either a shift of the electron pair connecting the carbon atom, holding the carboxyl group, to the carbon atom holding the *trans* phenyl group, or a shift of the electron pair connecting the carboxyl-carbon atom to the one holding the *cis* phenyl group can take place. The β- and ϵ-amino acids having their phenyl groups *cis* to each other give only the one expected product.[5] In the rearrangement of α- and δ-amino acids, it is noted that two products, the same in each case, are also formed. Compound III which predominates results from an inversion of configuration. Compound II, found only in small quantities, is the product expected from a retention of configuration during rearrangement. Thus, a small amount of racemization occurs in these two cases at carbon atom B. This fact would suggest a small amount of preliminary ionization of R :A:B:X:. Indeed this has been suggested in some of the original formulations of this electronic theory (1, 2 a, 16) of rearrangements.

We now wish to describe the results of certain experiments that we have carried out, and that serve both as an extention and as a confirmation of the results of Stoermer and his co-workers (15). They also give information that is fundamental to the modern theory of optical rotatory power as applied to ring compounds (17). The rearrangement of γ-truxillamic acid was repeated using, however, both the *dextro* and *levo* forms of the optically active acid instead of the racemic modification. In our hands the (−) amino acid hydrochloride[6] yielded the pure (+) lactone (IV) of the (+) acid (I), while the (−) lactone was obtained when the (+) amino acid hydrochloride was diazotized with nitrosyl bromide. These facts are in accord with theory. It is also to be noted that with the optically active modifications no contamination of the products of rearrangement with diastereomers produced by racemization at either carbon atom A or B was observed. This also is as we might expect, since here we are carrying out the rearrangement under asymmetric conditions.

[5] It may be noted that Stoermer and his co-workers observed that the products I, II, and III as described above were always contaminated with small amounts of the corresponding diastereomer. These products, of course, result from a certain amount of racemization on carbon atom A.

[6] The (−) γ-truxillamic acid used in these experiments was prepared from the (+) γ-truxillamidic acid by a Hofmann degradation. The (+) amidic acid was obtained from the racemic compound by a simple resolution involving one crystallization of the morphine salt. The action of aqueous ammonia upon racemic γ-truxillic acid anhydride yielded the corresponding amide. The anhydride was made by refluxing α-truxillic acid with acetic anhydride. Certain difficulties were noted in the preparation of α-truxillic acid which will be discussed in a subsequent paper. The method finally used was essentially the same as that described by Kohler, *Am. Chem. J.*, **28**, 238 (1902).

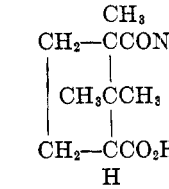
A number of reactions also were carried out starting with both the (+) and the (−) modifications of the lactone (IV). The results are listed in the accompanying chart, together with the molecular rotations of the various compounds which were prepared.



When these data are considered in terms of modern theory of optical rotatory power (17), the increase in the amount of rotation caused by the opening of the lactone ring is surprising, for Kauzmann and Eyring (17) have stated that "these influences which tend to restrict freedom of rotation and of orientation about bonds will tend to increase the order of magnitude of the optical activity." Thus, in general, hydroxy acids would be expected to have lower numerical

TABLE I

MOLECULAR ROTATIONS OF ACIDS AND THEIR CYCLIC DERIVATIVES

ACID	SOLVENT[a]	ACID $[M]_D$	ANHYDRIDE $[M]_D$	$(M_A)^-(M_A-H_2O)$[b]	REF
α-Isopropylglutaric	ether	(−) 27.5	(+) 5.6	+21.9	18
trans-Hexahydrophthalic	acetone	(+) 31.5	(−) 118.1	−86.6	19
trans-Δ^4-Tetrahydrophthalic	alcohol	(+) 196.0	(+) 10.0	+186	20
Camphoric	alcohol	(+) 192	(−) 14.0	+178	21
			Lactone		
2,2,3-Trimethyl-3[c]-cyclopentanol-1[c]-carboxylic	alcohol	(+) 87.5	(+) 13.1	+74.4	22
1,2,3-Trimethyl-3[c]-cyclopentanol-1[c]-carboxylic	alcohol	(+) 27.5	(−) 33.4	−5.9	23
α-(3-Methyl-3-cyclopentanol)-α,α-dimethylacetic	alcohol	(−) 6.5	(+) 29.5	−22.9	24
					
			Imide		
R = H	acetone	(+) 45	(−) 10.0	+35.1	21
n-C_5H_{11}	acetone	(+) 50.8	(+) 19.3	+31.5	
m-tolyl	acetone	(+) 89.0	(+) 47.0	+42.0	
α-naphthyl	acetone	(+) 24.2	(+) 80.7	−56.5	
β-naphthyl	acetone	(+) 210.9	(+) 55.2	+155.7	
			Lactam		
Aminocamphonanic	water	(−) 49.9	(−) 92.7	−42.8	25

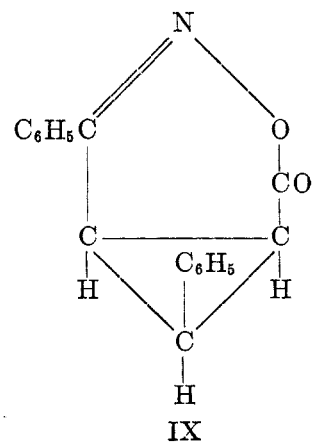
[a] Only compounds with which the rotations of both acid and anhydride have been taken in the same solvent are listed.

[b] Difference is numerical, not algebraic. The + indicates a higher value for the acid, the − for the anhydride.

molecular rotations than the corresponding lactones, since in the latter compounds rotation is more restricted. It is to be noted, however, that the examples given in Table I of their paper involve only the formation of monocyclic compounds from open chains, and that most of the substances listed are related to the sugars. Since in our case the noted exceptions involve the formation of a dicyclic system from a monocyclic derivative, it was thought pertinent to collect more data of this type. Some of these data are presented in Table I.

It is seen that in cases of this type the cyclization generalization of Kauzmann and Eyring (17) does not hold. It may be argued, however, that this failure does not affect the validity of the one electron theory of optical rotatory power, for if the rotatory power of the open chain compound be large, thus showing a considerable lack of asymmetry, cyclization would be much less likely to increase this asymmetry (26). It may be added that since monocyclic compounds, in general, have high rotations, which is in accord with theory, it is not surprising that shifts in rotation would be random on formation of the second ring.

In this connection it is of interest to consider another principle. It is seen from our experimental data that the (−) acid (I) is closely related configurationally to the (+) acid (III), the action of strong alkali converting the former compound into the latter. Since these two acids are so similar, one might think it possible to apply a principle analogous to the Freudenberg displacement rule (27) in order to demonstrate the configurational relationships involved. However, this can not be done. Although conversion of the acids to their respective keto esters causes a decrease in $[M]_D$, esterification of (I) results in a decrease in rotation, whereas the same reaction applied to (III) causes an increase. It is thus seen that no quantitative relationship in the shifts of the molecular rotations with similar chemical changes can be established. This is probably due to the close proximity (28) of the groups to each other. Indeed, this closeness of the groups attached to different carbon atoms in the cyclopropane ring is shown by the ease with which acid (I) is converted into its lactone (IV). If one acidifies the sodium salt of the acid with sulfuric acid, the lactone is produced on crystallization, no matter what the conditions are for carrying out the process. Only when hydrochloric acid is used does one get the hydroxy acid itself. Furthermore, under certain conditions the action of diazomethane brings about a dehydration to the lactone, a phenomenon that has also been observed in the sugars (29) and in folded rings of the bicyclo-(1,2,2)-heptane series (30). Finally, it may be noted that the keto ester (VI) is unusual in its behavior. Although actually a γ-keto ester, its reaction with hydroxylamine hydrochloride is similar to that undergone by 3-keto esters in the preparation of isoxazolones. Instead of an oxime, a cyclic dihydroörthoxazine derivative (IX) is produced, again indicating the closeness of groups on adjacent carbon atoms in the cyclopropane nucleus.



IX

EXPERIMENTAL

Preparation of (+) and (−) γ-truxillamidic acids. The optically active acids were prepared from the racemic modification by the method of Stoermer and Fretwurst (31). Racemic-γ-truxillamidic acid, m.p. 233–236°, was prepared in 75% yield according to the directions of these authors from α-truxillic acid, m.p. 274–276° (decomp.), which in turn, was prepared in 35% yield by the method of Kohler[6] from cinnamylidene malonic acid (32), m.p. 196–200°. From 18.7 g. of racemic acid was obtained 7.7 g. of (−) γ-truxillamidic acid, $[\alpha]_D^{20}$ −7° (*c* = 0.76, acetic acid), m.p. 254–256° when placed in the bath at 243°, and also 5.6 g. of (+) γ-truxillamidic acid, $[\alpha]_D^{20}$ +8° (*c* = 0.75, acetic acid). Stoermer and Fretwurst (31) report for the (−) acid $[\alpha]_D^{20}$ −11° (*c* = 0.70, acetic acid). In view of the inaccuracies attending the determination of this constant for a substance of such low rotatory power and slight solubility, we do not regard the discrepancy as serious. Moreover, the character of the products obtained from reactions of the acid which are subsequently to be described, indicated that it was essentially optically pure.

Preparation of (−) γ-truxillamic acid. This acid was prepared by a method analogous to that of Stoermer (15) for the preparation of the racemic acid. To 10.3 g. of (+) γ-truxillamidic acid was added 145 cc. of 0.5 *N* sodium hypochlorite solution. The reaction mixture was kept at 38–40° for two hours. At the end of this time it was cooled to room temperature, neutralized with dilute hydrochloric acid, and finally made just basic to litmus with dilute sodium hydroxide solution. The solution was filtered to remove a very small amount of insoluble material (m.p. 200–225°), and carbon dioxide was then passed through the filtrate until a precipitate began to form (at this point, if too much sodium hydroxide solution had been added, it was sometimes necessary to add a few drops of hydrochloric acid to induce precipitation). Carbon dioxide was passed through the solution for an additional hour, after which time 7.7 g. of pure (−) γ-truxillamic acid had separated. The product melted at 211–214° (decomp.) when placed in the bath at 200° and was insoluble in most solvents. Acidification of the aqueous mother liquor produced a white precipitate, which after recrystallization melted at 250° (decomp.) and was shown by a mixed melting point determination to be unchanged (+) γ-truxillamidic acid. Similar treatment of (−) γ-truxillamidic acid gave (+) γ-truxillamidic acid in 65% yield.

A small portion of the (−) amino acid on recrystallization from dilute hydrochloric acid was converted to the corresponding hydrochloride, m.p. 268° (decomp.); $[\alpha]_{6563}^{20}$ −16.6°, $[\alpha]_{5893}^{20}$ −22.7°, $[\alpha]_{5463}^{20}$ −28.8° (*c* = 1.145, methyl alcohol). From the analysis it is apparent that the crystalline salt contains one molecule of water of crystallization.

Anal. Calc'd for $C_{17}H_{18}ClNO_2$: C, 67.24; H, 5.94; N, 4.61.
Calc'd for $C_{17}H_{18}ClNO_2 \cdot H_2O$: C, 63.46; H, 6.28; N, 4.35.
Found: C, 63.90; H, 6.33; N, 4.28.

The (−) amino acid hydrochloride was readily converted to the corresponding methyl ester on being refluxed for three hours in a methyl alcoholic solution of hydrogen chloride. The ester, after recrystallization from methyl alcohol, melted at 269° (decomp.) when placed in the bath at 250°; $[\alpha]_{6563}^{20}$ −24.7°, $[\alpha]_{5893}^{20}$ −29.6°, $[\alpha]_{5463}^{20}$ −36.8° (*c* = 1.12, methyl alcohol).

Anal. Calc'd for $C_{18}H_{20}ClNO_2$: C, 68.05; H, 6.30; N, 4.41.
Found: C, 68.03; H, 6.27; N, 4.48.

Rearrangement of (+) γ-truxillamic acid to the lactone (IV). To 7 g. of (+) γ-truxillamic acid just covered with ether in an ice-salt-bath, was slowly added a solution of nitrosyl bromide [prepared by passing nitric oxide (33) into 200 cc. of dry ether containing 5.6 g. of bromine at −5°]. During the addition the temperature was kept below −5°. Vigorous evolution of nitrogen attended the addition of the first 100 cc. of solution, but the remainder could be added rather rapidly without an appreciable increase in temperature. When the evolution of nitrogen had ceased (about one hour after addition was complete), the white needles which had formed were removed by filtration, washed with ether, and dried: m.p. 133–135°. The dark brown ether solution was shaken with sodium bisulfite until colorless. The bisulfite layer was then extracted with ether and the combined ether extracts washed with dilute sodium carbonate. The carbonate layer was extracted with ether, and the

united ether extracts were dried over anhydrous potassium carbonate. On evaporation of the ethereal solution to a volume of 20 cc., an additional crop of crystals, m.p. 133–135°, was obtained. Finally the ether was removed from the mother liquor. The oil so obtained partially solidified on standing. The crystals were separated from the oil by filtration and washed with a small amount of ether. The three crops of crystals were united and recrystallized from benzene-petroleum ether (b.p. 60–75°) to give 3.08 g. of a pure product, m.p. 139°; $[\alpha]^{20}_{6563}$ −10.2°, $[\alpha]^{20}_{5893}$ −14.4°, $[\alpha]^{20}_{5463}$ −19.5°, $[M]^{20}_{D}$ −36.0° (c = 1.07, methyl alcohol); $[\alpha]^{20}_{6563}$ +30.6°, $[\alpha]^{20}_{5893}$ +35.2°, $[\alpha]^{20}_{5463}$ +41.8° (c = 1.05, benzene).

Anal. Calc'd for $C_{17}H_{14}O_2$: C, 81.59; H, 5.65.
Found: C, 81.8; H, 5.68.

Similar treatment of (−) γ-truxillamic acid gave the (+) lactone in 43% yield, m.p. 138°; $[\alpha]^{20}_{6563}$ +11.2° $[\alpha]^{20}_{5893}$ +15.5°; $[\alpha]^{20}_{5463}$ +19.6°, $[M]^{20}_{D}$ +38.7° (c = 1.25, methyl alcohol). Mixed m.p. of the (+) and (−) lactones 129–131°.

Preparation of 1c-carboxy-2c-benzoxyl-3c-phenylcyclopropane (I). A mixture of 1.15 g. of the (−) lactone (IV) and 8 cc. of 10% alcoholic potassium hydroxide was heated for one minute longer than necessary to effect complete solution. It was then diluted with 35 cc. of water and filtered. The filtrate was carefully neutralized with dilute hydrochloric acid and the resulting precipitate separated by filtration, washed thoroughly with water, and dried. After two recrystallizations from benzene the product melted at 150° (decomp.) when placed in the bath at 141°; $[\alpha]^{20}_{6563}$ −78.4°, $[\alpha]^{20}_{5893}$ −101.4°, $[\alpha]^{20}_{5463}$ −121.4°, $[M]^{20}_{D}$ −272° (c = 1.02, methyl alcohol).

Anal. Calc'd for $C_{17}H_{16}O_3$: C, 76.14; H, 5.97.
Found: C, 75.80; H, 6.14.

Similar treatment of the (+) lactone (IV) gave the hydroxy acid (I) m.p. 146°; $[\alpha]^{20}_{6563}$ +75.4°, $[\alpha]^{20}_{5893}$ +96.6°, $[\alpha]^{20}_{5463}$ +116.6°, $[M]^{20}_{D}$ −259° (c = 1.18, methyl alcohol).

Action of diazomethane on the hydroxy acid (I). To a methyl alcoholic solution of the (−) acid (I) at the temperature of an ice-salt mixture was added slowly and with shaking an ethereal solution of diazomethane (34) until no more nitrogen was evolved, and the yellow color due to a slight excess of diazomethane was permanent. The solution was removed from the ice-salt-bath, allowed to stand for thirty minutes, and evaporated to dryness.

The residue was recrystallized from aqueous methyl alcohol: m.p. 137–139°; $[\alpha]^{20}_{6563}$ −10.6°, $[\alpha]^{20}_{5893}$ −14.9°, $[\alpha]^{20}_{5463}$ −20.1° (c = 1.04, methyl alcohol); mixed m.p. with the (−) lactone (IV) 137–139°. The same result was obtained when the foregoing operations were repeated, and also when an ethereal solution of diazomethane, distilled from anhydrous potassium hydroxide just before use, was employed.

In another experiment a solution of the acid was prepared in 20 cc. of methyl alcohol containing 5 drops of water, and to it was added according to the procedure described above, a distilled ethereal solution of diazomethane. The product so obtained was recrystallized from benzene-petroleum ether: m.p. 145° (decomp.); $[\alpha]^{20}_{6563}$ −89.4°, $[\alpha]^{20}_{5893}$ −118.5°, $[\alpha]^{20}_{5463}$ −141.7°, $[M]^{20}_{D}$ −334° (c = 1.27, methyl alcohol). By analysis and subsequent oxidation this product was proved to be the desired (−) methyl ester (V).

Anal. Calc'd for $C_{18}H_{18}O_3$: C, 76.60; H, 6.39.
Found: C, 76.80; H, 6.54.

The same product was obtained by the addition of ethereal diazomethane to an anhydrous ethereal solution of the acid, but the reaction was much slower.

In another experiment careful trituration with boiling petroleum ether (b.p. 60–75°) of the crude product resulting from the treatment of the (+) acid (I) in methyl alcoholic solution as described above, permitted separation of this product into two fractions. The more insoluble of these melted at 146° and was the desired (+) ester (V): $[\alpha]^{20}_{6563}$ +95°, $[\alpha]^{20}_{5893}$ +127°, $[\alpha]^{20}_{5463}$ +140°, $[M]^{20}_{D}$ +358° (c = 0.295, methyl alcohol).

Anal. Calc'd for $C_{18}H_{18}O_3$: C, 76.60; H, 6.39.
Found: C, 76.77; H, 6.39.

The more insoluble fraction melted at 115°. Analysis and specific rotation indicated

that it was an equimolar mixture of the lactone (IV) with the ester (V): $[\alpha]^{20}_{6563}$ +53.6°, $[\alpha]^{20}_{5893}$ +73.1°, $[\alpha]^{20}_{5463}$ +87.9° (c = 0.673, methyl alcohol).

Anal. Calc'd for $C_{18}H_{18}O_3 \cdot C_{17}H_{14}O_2$: C, 78.90; H, 6.06.
Found: C, 78.78; H, 6.22.

Preparation of the (+) methyl ester (VI) of 1^c-carboxy-2^c-benzoyl-3^c-cyclopropane. To 480 mg. of the (−) methyl ester (V) was added 250 mg. of chromic oxide in 5 cc. of glacial acetic acid. The mixture was cooled slightly at first and then allowed to stand at room temperature with frequent shaking for forty-eight hours. At the end of this time 60 cc. of water was added, causing the formation of a precipitate. The mixture was extracted with ether and the ether extract washed with sodium carbonate solution and dried over anhydrous sodium sulfate. Evaporation of the solution to a volume of 8 cc. followed by the addition of petroleum ether (b.p. 60–75°) caused the precipitation of a crystalline product, m.p. 95–110°. One recrystallization from ether gave the pure keto ester (VI): m.p. 109°; $[\alpha]^{20}_{6563}$ +5.4°, $[\alpha]^{20}_{5893}$ +6.0°; $[\alpha]^{20}_{5463}$ +7.21, $[M]^{20}_{D}$ +16.8° (c = 0.833, methyl alcohol).

Anal. Calc'd for $C_{18}H_{16}O_3$: C, 77.16; H, 5.72.
Found: C, 77.11; H, 5.61.

Preparation of the (+) dihydroörthoxazine (IX) of the (+) keto ester (VI). The (+) keto ester (VI) was refluxed for one day in 15 cc. of ethyl alcohol containing an excess of hydroxylamine hydrochloride. On cooling, the solution deposited long white needles, m.p. 177–179°. One recrystallization from methyl alcohol gave a product melting at 180°; $[\alpha]^{20}_{6563}$ +177°, $[\alpha]^{20}_{5893}$ +226°, $[\alpha]^{20}_{5463}$ +271°, $[M]^{20}_{D}$ +595° (c = 0.223, methyl alcohol). The analysis indicated that the product was a dihydroörthoxazine rather than an oxime:

Anal. Calc'd for $C_{18}H_{16}NO_3$: C, 73.21; H, 5.81; N, 4.74.
Calc'd for $C_{17}H_{13}NO_2$: C, 77.56; H, 4.99; N, 5.32.
Found: C, 77.87; H, 4.95; N, 5.25.

Preparation of 1^t-carboxy-2^c-benzoxyl-3^c-phenylcyclopropane (III). A solution of 900 mg. of the (−) lactone (IV) in 8 g. of 50% alcoholic potassium hydroxide was refluxed for ninety minutes and then evaporated almost to dryness. The residue was taken up in water, and the clear aqueous solution was acidified with dilute hydrochloric acid. The precipitate which resulted was recrystallized three times from dilute alcohol: m.p. 160° (decomp.); $[\alpha]^{20}_{6563}$ +43.2°, $[\alpha]^{20}_{5893}$ +56.4°, $[\alpha]^{20}_{5463}$ +68.3°, $[M]^{20}_{D}$ +151° (c = 1.13, methyl alcohol).

Anal. Calc'd for $C_{17}H_{16}O_3$: C, 76.14; H, 5.97.
Found: C, 76.13; H, 5.92.

Similar treatment of the (+) lactone (IV) gave the corresponding (−) acid (III): m.p. 161–162° (decomp.); $[\alpha]^{20}_{6563}$ −43.3°; $[\alpha]^{20}_{5893}$ −56.0°, $[\alpha]^{20}_{5463}$ −67.8° $[M]^{20}_{D}$ −150° (c = 1.10, methyl, alcohol).

Esterification of these acids with diazomethane gave the corresponding methyl esters (VII) as oils.

Methyl ester of the (+) acid, $[\alpha]^{20}_{6563}$ +47.3°, $[\alpha]^{20}_{5893}$ +60.6°, $[\alpha]^{20}_{5463}$ +73.2°, $[M]^{20}_{D}$ = +171° (c = 2.15, methyl alcohol).

Methyl ester of the (−) acid, $[\alpha]^{20}_{6563}$ −47.4°, $[\alpha]^{20}_{5893}$ −61.4°, $[\alpha]^{20}_{5463}$ −74.9°, $[M]^{20}_{D}$ −173° (c = 1.19, methyl alcohol).

Methyl alcoholic solutions of the (+) and (−) esters were mixed to give a solution of zero rotation. Evaporation of this solution gave the racemic ester, which after one recrystallization from ether-petroleum ether melted at 75° (Stoermer (15) reports m.p. 76°).

Preparation of the (−) methyl ester (VIII) of 1-carboxy-2-benzoyl-3-phenylcyclopropane. To the methyl ester (VII) prepared from 500 mg. of the (+) lactone (IV) was added a solution of 250 mg. of chromic oxide in 12 cc. of acetic acid. The mixture was heated on the steam-bath until the solution became green and was then diluted with 60 cc. of water. The resulting oil was extracted from the mixture with ether. The ether extract was washed with sodium carbonate solution and dried over anhydrous sodium sulfate. On evaporation of the ethereal solution an oil was obtained which was dissolved in 5 cc. of methyl alcohol and decolorized with animal charcoal. Evaporation to dryness of the clear solution so obtained gave an oil which gradually became crystalline. After one recrystallization from

ether-petroleum ether the product melted at 85°; $[\alpha]^{20}_{6563}$ −121.2°, $[\alpha]^{20}_{5893}$ −158.6°, $[\alpha]^{20}_{5463}$ −192.5°, $[M]^{20}_{D}$ −444° (c = 0.974, methyl alcohol).

Anal. Calc'd for $C_{18}H_{16}O_3$: C, 77.16; H, 5.72.
Found: C, 77.07; H, 5.63.

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SUMMARY

(+) γ-Truxillamic acid has been shown to yield, on treatment with nitrosyl bromide, the (−) lactone of (−) 1^c-carboxy-α^c-benzoxyl-3^c-phenylcyclopropane. This result and other examples of Walden inversion attending the conversion of truxillamic and truxinamic acids to 1-carboxy-2-benzoxyl-3-phenylcyclopropanes are considered in terms of the electronic theory of molecular rearrangements.

The direction of the shift in optical rotatory power in the formation of dicyclic lactones, imides, and lactams from the corresponding monocyclic acids has been shown to be random. This behavior is discussed in the light of newer theories of optical rotatory power.

The preparation and certain reactions of the optically active *cis*- and *trans*-1-carboxy-2^c-benzoxyl-3^c-phenylcyclopropanes are described.

PRINCETON, N. J.

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