

Preparation of Dibromohydroxybenzylphenol.—17.2 g. of dibromosaligenin bromide was dissolved in 250 cc. of hot toluene in a 500-cc. round-bottomed, three-necked flask, fitted with mechanical stirrer, reflux condenser, and dropping funnel. A small piece of mossy zinc, previously cleaned by hydrochloric acid, was added, followed by 7.0 g. of phenol in 50 cc. of toluene. The mixture was then heated to boiling until the evolution of hydrogen bromide had practically ceased (about three hours). The toluene solution was then washed with water to remove hydrogen bromide, dried with anhydrous sodium sulfate and concentrated *in vacuo*. The solution was then diluted with one-half its volume of ligroin and cooled in the ice-box. The crystals thus obtained were recrystallized from toluene.

Preparation of Dibromohydroxybenzyl dibromophenol.—5.0 g. of dibromohydroxybenzylphenol, prepared as described above, was dissolved in 50 cc. of warm glacial acetic acid and 5 g. of bromine added drop by drop. The solution was allowed to stand at room temperature for several hours and finally cooled in ice. The resulting white crystals were recrystallized from acetic acid.

Preparation of Dibromohydroxybenzyl Phenyl Ether.—The filtrate from the preparation of dibromohydroxybenzylphenol was steam distilled to remove the toluene and ligroin. The resulting heavy oil was crystallized repeatedly from dilute alcohol. After refluxing for three hours with acetic anhydride in the presence of anhydrous sodium acetate, this compound yielded only a mono-acetate, indicating the formula assigned it.

The author wishes to acknowledge the valuable assistance of Mr. Grant Spurrier, who performed many of the analyses.

Summary

1. A number of derivatives of dibromosaligenin bromide have been prepared.
2. A preliminary investigation indicates that certain of these derivatives possess valuable pharmacological properties.

BALTIMORE, MARYLAND

RECEIVED JUNE 17, 1933
PUBLISHED OCTOBER 6, 1933

[CONTRIBUTION No. 91 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Occurrence of a New Case of Isomerism in the Fluorenone Carboxylic Acid Series: Isomeric Products from the Action of Sulfuric Acid upon 3,3'-Dichlorodiphenic Acid

BY ERNEST H. HUNTRESS, IVAN S. CLIFF AND EDWARD R. ATKINSON

The Effect of Acetic Anhydride and of Concentrated Sulfuric Acid upon 3,3'-Dichlorodiphenic Acid.—In the course of some work upon 3,3'-dichlorodiphenic acid¹ we had occasion to examine its behavior with acetic anhydride and with concentrated sulfuric acid. With the former it readily yielded a monomolecular anhydride which has been reported in the earlier paper. Upon turning to the action of sulfuric acid, however, we found that two distinct but isomeric products were formed according to the temperature employed. One of these substances (formed at 125°) appears to be

(1) Huntress and Cliff, *THIS JOURNAL*, **55**, 2559-2567 (1933).

the expected keto acid for it titrates readily, easily forms the corresponding acid chloride and amide, and on heating loses carbon dioxide to give a dichlorofluorenone. The details of this behavior have also been described in the cited reference.

The product obtained at a higher temperature (170°), however, appears also to be a dichlorofluorenone carboxylic acid. Its analysis for chlorine is identical with that of the expected keto acid, its molecular weight is the same as that of the isomeric keto acid, and it definitely contains a carboxyl group as shown by the formation of an acid chloride and an amide. Moreover, it certainly contains a ketone group for not only is it colored yellow like other fluorenone carboxylic acids but it readily yields an oxime. We have, therefore, two isomeric monobasic acids prepared at different temperatures by the same procedure from the same starting material when the conventional theory will account for only one. For reasons which will appear we choose to regard as the true keto acid that dichlorofluorenone carboxylic acid obtained at the lower temperature; the isomer produced at the higher temperature we have temporarily designated as "Acid X."

It is a surprising fact that these two isomeric acids melt without evidence of decomposition at exactly the same temperature (242.5° uncorr.); nevertheless the melting range of approximately equal parts of the two individuals is broad and far depressed, *viz.*, 205–208°, 195–200°, 200–205° in various experiments. The conviction that these two acids are really different individuals is furthermore supported by their conversion to analytically isomeric acid chlorides which melt at slightly different temperatures and depress each others melting points, and the conversion of these acid chlorides to the corresponding amides which in turn give identical analyses and have different melting points but whose mixture fuses far below that of either individual. These facts are included in the following Table I.

TABLE I
MELTING POINTS AND MIXED MELTING POINTS

Parent substance	Acid	Acid chloride	Acid amide
A Keto acid (from 3,3'-dichlorodiphenic acid)	242.5	180–181	280–281
B Mixtures of A and C	205–208	195–200	200–205
C "Keto acid X"	242.5	140–145	255–260
D Mixtures of C and E	235–239	183–184	296
E "Hunn's keto acid" (from 5-5'-dichlorodiphenic acid)	240	178–180	292–294
F Mixtures of A and E	205–208	185	301
		145–150	150–155
			250–252

During the early part of the work the two isomeric acids had been recrystallized from different solvents and it was thought possible that they were different crystalline forms. Interchange of solvents, however, effected no change in original melting point nor upon the melting point of the mixture. Furthermore, when the keto acid formed at 125° was redissolved in

sulfuric acid and heated under the same conditions which were known to yield "Acid X" directly from the original 3,3'-dichlorodiphenic acid, there was isolated a good yield (67%) of resultant product which was identical with "Acid X" as evidenced by its depression of the melting point of the keto acid and its failure to depress the melting point of a sample of "Acid X" prepared in the usual manner. It thus is evident that the keto acid can be converted into "Acid X."

We are inclined to regard as the "true" keto acid that produced at the lower temperature on three principal grounds. First it titrates very smoothly in neutral alcohol yielding neutralization equivalents which closely check the theoretical, whereas "Acid X," although soluble in alkalis and even in sodium bicarbonate solution, behaves very strangely when titrated in alcohol, giving poor end-points and erratically variant numerical results. Second, on heating above its melting point the keto acid obtained at the lower temperature smoothly evolves carbon dioxide and yields as principal product 1,6-dichlorofluorenone, whereas "Acid X" under precisely the same conditions sublimes almost unchanged. Third, since the so-called "Acid X" appears to be preparable from the so-called keto acid it seems probable that any abnormal rearrangement would be produced at the higher temperature rather than at the lower.

In speculating as to the probable reason for the appearance of two isomeric series of derivatives, the first thought is that the "Acid X" might be the corresponding anhydride of the 3,3'-dichlorodiphenic acid produced by the dehydrating action of the sulfuric acid. That this cannot be the explanation, however, is evidenced by the previous preparation of this product in normal fashion. It was colorless, melted at 257-258° uncorr., gave correct analysis for chlorine, did not dissolve in sodium carbonate solution, did dissolve in an alkali, and these solutions on acidification reprecipitated 3,3'-dichlorodiphenic acid. Furthermore the melting point of a mixture of "Acid X" with this authentic anhydride was markedly depressed. A second suggestion that "Acid X" might be the bimolecular anhydride of the keto acid formed from 3,3'-dichlorodiphenic acid at 125° is also inadmissible, for a determination of its molecular weight in camphor yielded a result consistent only with the presence of one fluorenone nucleus. A third hypothesis would ascribe the supposed isomer to the presence in the original raw material of another isomeric dichlorodiphenic acid. Against this view we can urge the following considerations. 1. The 3,3'-dichlorodiphenic acid was carefully purified. Moreover it had been prepared by a series of synthetic steps in which each intermediate had been carefully purified. The original commercial intermediate from which the series had started was a homogeneous material. 2. The yields of "Acid X" readily obtainable were such as to preclude the possibility of its origin from an impurity. For example, 31% of pure product was obtained after reprecipi-

tation from sodium bicarbonate solution and recrystallization from glacial acetic acid.

Since carbon dioxide could not be eliminated from "Acid X" either by heating alone or with soda lime, the carboxyl group was finally replaced by hydrogen by means of conversion of the amide to the amine, diazotization and boiling with alcohol. This series of operations yielded 1,6-dichlorofluorenone identified by analysis, by melting point, by mixed melting point with an authentic sample, by conversion to the oxime and mixed melting point of the latter with an authentic specimen. This result shows that during the isomerization to "Acid X" both the fluorenone nucleus and the relative position of the two halogen atoms in it are preserved.

The Effect of Acetic Anhydride and of Concentrated Sulfuric Acid upon 5,5'-Dichlorodiphenic Acid.—When 5,5'-dichlorodiphenic acid is refluxed with acetic anhydride the corresponding diphenic anhydride readily forms in good yield.² In an earlier paper we have shown³ that at 400° this anhydride evolves carbon dioxide and yields 3,6-dichlorofluorenone.

Upon heating 5,5'-dichlorodiphenic acid with concentrated sulfuric acid at 125°, *i. e.*, under the same conditions which transformed 3,3'-dichlorodiphenic acid to the keto acid condensation product, we have obtained here also a keto acid which, although not reported by him, may conveniently be designated as "Hunn's keto acid." Although this substance yielded a corresponding acid chloride and amide and the melting points both of the acid and of its derivatives are of the same general magnitude as those noted for the products from the 3,3' series, yet the melting points of mixtures of corresponding compounds of the "Acid X" series and the Hunn's keto acid series were slightly though definitely depressed. This observation appears to eliminate the possibility that the formation of "Acid X" might be due to the presence of 5,5'-dichlorodiphenic acid or its reaction products in the original material. Furthermore, the melting points of mixtures of compounds of the keto acid series with the corresponding compounds of the Hunn's keto acid series were greatly depressed. These observations are all included in Table I.

The Examination of Other Dichlorodiphenic Acids for Possible Isomeric Keto Acids.—Having observed this formation of isomeric materials in the sulfuric acid treatment of 3,3'-dichlorodiphenic acid, we have also examined in a preliminary way the possibility that an analogous situation would appear with other dichlorodiphenic acids. Of the three other possible symmetrically substituted dichlorodiphenic acids, we already had available a sample of the 5,5'-dichloro isomer from another part of the work. A sample of 6,6'-dichlorodiphenic acid prepared according to the method of Christie, James and Kenner⁴ was made available to us through the cour-

(2) Hunn, *THIS JOURNAL*, **45**, 1024-1030 (1923).

(3) Ref. 1, p. 2566.

(4) Christie, James and Kenner, *J. Chem. Soc.*, **123**, 1948 (1923).

tesy of Prof. A. A. Morton. 4,4'-Dichlorodiphenic acid, not previously reported in the literature, was synthesized from 5-chloro-2-aminobenzoic acid by the same method used for the 3,3'-isomer.

With the 4,4'- and the 5,5'- isomers the reaction product obtained by the action of concentrated sulfuric acid at 125° appeared to be the same as the product obtained at 175° in the respective cases. The corresponding keto acid was formed in each instance but the melting point of mixtures of the products from different temperatures was not depressed. It will be noted that in the case of 6,6'-dichlorodiphenic acid there would presumably be no possibility of fluorenone carboxylic acid formation by a ring closure process, for the necessary positions are filled with chlorine atoms. As a matter of fact we found that this 6,6'-dichlorodiphenic acid when heated with concentrated sulfuric acid at 175° for thirty minutes gave only a slight coloration in the resultant solution, evolved no gas, and was recovered unchanged upon dilution.

Experimental Part

All melting points reported in this paper were taken by the method described in Mulliken's "Identification of Pure Organic Compounds," Vol. I, page 218, on a 360° rod form melting point thermometer immersed in the sulfuric acid to the 0° point.

3,3'-Dichlorodiphenic Acid.—This acid was prepared exactly as described in an earlier paper.⁵

The New Keto Acid from 3,3'-Dichlorodiphenic Acid. ("Acid X.")—Two grams of 3,3'-dichlorodiphenic acid (m. p. 299–300°) was added to 5 ml. of pure concentrated sulfuric acid in a small flask and heated in an oil-bath at 170 ± 1° for one hour. The deep reddish-brown solution was observed to give off bubbles of gas during the heating. Finally, the sulfuric acid solution was poured onto cracked ice and the grayish-yellow precipitate filtered off, washed with water until free from sulfate and dried at 110°. The crude product melted at 195–200° and weighed 1.88 g. corresponding to a quantitative yield of keto acid. For purification it was dissolved in 100 ml. of 1 *N* sodium bicarbonate solution at 50°, filtered, and reprecipitated by acid. Only a trace of insoluble material remained and 1.8 g. of acid was reprecipitated from the alkaline solution. Recrystallization from hot glacial acetic acid after brief treatment with Norite decolorizing carbon yielded 1.0 g. of yellowish-gray product, m. p. 241°. Repeated recrystallization from hot glacial acetic acid will raise the melting point to 242.5° uncorr.

The results of analysis and molecular weight were as follows: *Anal.* Calcd. for C₁₄H₈Cl₂O₃: Cl, 24.23. Found: 24.47, 24.30; on a different sample, 24.32, 24.16. Calcd.: C, 57.34; H, 2.05. Found: C, 57.45, 57.41; H, 2.55, 2.51. *Mol. wt.* (Rast method in camphor) Calcd., 293. Found: 300, 290, 290.

All attempts to get consistent results on titration of "Acid X" have so far been unsuccessful. Titrated directly in aqueous suspension with *N*/10 sodium hydroxide using phenolphthalein gave values of 316.1 and 314.5. The same sample dried at 110° for two hours and titrated in neutral alcohol gave 299.8 and 301.4. After recrystallizing the sample twice from glacial acetic acid and repeating the titration in alcohol, the values obtained were 283.6 and 281.1. After still another recrystallization from glacial acetic acid the neutralization equivalents in alcohol were 266.4, 274.7 and 266.6. None of these values come very near the theoretical of 293. The titration liquors from these

(5) Ref. 1, p. 2561.

last three runs were combined, acidified, and the precipitated acid recrystallized from glacial acetic acid: the product melted 242.5–243.0° as in the first place. A different sample of "Acid X" similarly titrated in alcohol gave values of 285.8 and 285.6. If dissolved in excess standard sodium hydroxide by heating at 90° for one minute and measured by titrating the excess alkali, this sample gave values of 275.2 and 281.1. In all the above titrations phenolphthalein was employed. The end-point was very indefinite and difficult to fix with certainty, contrasting sharply with the normal precise end-point noted with the isomeric keto acid of our earlier paper.⁶

It will be recalled that the melting point of the keto acid obtained from 3,3'-dichlorodiphenic acid by the action of sulfuric acid at 125° was observed to be 242.5° and that the corresponding constant for the "Acid X" obtained in a similar manner at 170° is precisely the same, *viz.*, 242.5°. Nevertheless, mixtures of equal weights of the two isomeric substances were strongly depressed and the effect was confirmed in three separate experiments, the melting range of the mixture being observed at 205–208°, 195–200° and 200–205°, respectively.

Since the keto acid had been recrystallized from alcohol, while the "Acid X" had been purified from glacial acetic acid, an experiment was made to determine whether interchange of solvents would have any effect. For this purpose a sample of pure keto acid (previously prepared from alcohol) was recrystallized from hot glacial acetic acid; and a sample of pure "Acid X" (previously prepared from acetic acid) was recrystallized from hot alcohol with addition of water. After this procedure each recovered product possessed its original melting point and did not depress the melting point of its corresponding original. Mixtures of the recrystallized keto acid and "Acid X," however, showed the same marked depression of melting point observed in the original samples.

Conversion of Keto Acid to "Acid X."—A sample of 1.65 g. of absolutely pure keto acid, m. p. 242.0–242.5°, prepared at 125° was redissolved in 4.0 ml. of pure concentrated sulfuric acid and heated for one hour at 170 ± 1° (*i. e.*, under the conditions which had yielded "Acid X"). The yield of crude was 1.4 g., m. p. 212–215° dec.; after dissolving in sodium bicarbonate solution without appreciable residue acidification threw down 1.2 g. of dull yellow solid, m. p. 220–225° dec. After recrystallization from glacial acetic acid there was obtained 1.1 g. of light yellow acid, m. p. 241–242°. This sample failed to depress the melting point when mixed with authentic "Acid X," but depressed that of an authentic sample of keto acid to 203–205°.

The Acid Chloride of "Acid X."—One and three-tenths grams of pure "Acid X," m. p. 242.5°, was refluxed for two hours with 5.3 g. of pure thionyl chloride. On cooling the clear solution deposited bright yellow crystals, m. p. 183–184° uncorr. This melting point was unchanged upon further recrystallization from anhydrous benzene.

Anal. Calcd. for C₁₄H₅Cl₃O₂: Cl, 34.19. Found: 34.31, 34.10.

The melting point of a mixture of approximately equal parts of the keto acid chloride (m. p. 180–181°) with the "Acid X" chloride (m. p. 183–184°) was depressed to 140–145°.

The Amide of "Acid X."—A small sample (0.4 g.) of pure acid chloride from "Acid X" was shaken with excess concentrated ammonium hydroxide in the cold, and the insoluble residual solid filtered and washed with water. Recrystallization from hot alcohol by partial precipitation with water gave the amide (0.3 g.) as a cream colored solid, m. p. 296° uncorr.

Anal. Calcd. for C₁₄H₇Cl₂NO₂: Cl, 24.29. Found: 24.45, 24.62.

The melting point of a mixture of equal parts of the keto acid amide (m. p. 280–281°) with the "Acid X" amide (m. p. 296°) was depressed to 255–260°.

(6) Ref. 1, p. 2564.

The Oxime of "Acid X."—Three-tenths of a gram (0.001 mole) of "Acid X" (m. p. 242.5°) was dissolved in 5 ml. of 1 *N* sodium bicarbonate and a solution of 0.43 g. (0.010 mole) of hydroxylamine hydrochloride in 5 ml. of alcohol was added. After refluxing for fifteen minutes 50 ml. of water was added to the clear solution, precipitating 0.28 g. (85% theoretical) of cream colored oxime. After dissolving in 10 ml. of acetone and reprecipitating with 10 ml. of hot water the melting point remained constant at 286° dec. uncorr.

Anal. Calcd. for $C_{14}H_7Cl_2NO_3$: Cl, 23.02. Found: 22.92, 22.92.

The substance is difficultly soluble in cold ether or hot water, slightly soluble in alcohol, very soluble in acetone.

The Amine from "X Acid" Amide.—One and six-tenths grams (0.0055 mole) of "X acid" amide was made into a smooth paste with 20 ml. of water. This paste was then added to a solution of sodium hypobromite prepared from 1.3 g. (0.0081 mole) of bromine, 3.0 g. (0.075 mole) of sodium hydroxide, and 20 ml. of water and the ice cold mixture allowed to stand for two hours. After filtering off a small amount of undissolved solid, the red-brown filtrate was heated at 100° for two hours causing the precipitation of a brick-red crude weighing 0.82 g. (57% theoretical) and melting 245–255° uncorr. This melting point was unchanged by recrystallization from alcohol, but after boiling with alcoholic sodium hydroxide for twenty minutes a homogeneous red solid, m. p. 229–230° uncorr., was obtained.

Anal. Calcd. for $C_{13}H_7Cl_2NO$: Cl, 26.90. Found: 27.36, 26.95.

The melting point of a mixture of this amine with that from 1,6-dichlorofluorenone-5-carboxylic acid amide (keto acid amide) was depressed to about 190°.

1,6-Dichlorofluorenone from the Amine Corresponding to "Acid X."—Three-tenths gram (0.0114 mole) of the above amine was suspended in 30 ml. of alcohol and treated with 3 ml. of concentrated hydrochloric acid plus 2 ml. of water. Much of the amine dissolved in the alcohol to give a solution which turned grayish-yellow on addition of acid. To the ice cold mixture was slowly added a concentrated solution of 0.1 g. of sodium nitrite until a definite excess was noted. After standing for thirty minutes, 0.1 g. of copper bronze was added and the mixture allowed to stand overnight. The next morning 0.24 g. (85% theoretical) of crude 1,6-dichlorofluorenone melting at 205–206° was filtered off. After one recrystallization from benzene and subsequent vacuum sublimation, 0.15 g. of pure ketone melting at 217.5° uncorr. was obtained.

Anal. Calcd. for $C_{13}H_6Cl_2O$: Cl, 28.48. Found: Cl, 28.46, 28.28.

A mixture of the above product with authentic 1,6-dichlorofluorenone also melted at 217.5° uncorr. As final proof of the identity of the compound it was converted to the oxime in the usual manner. This melted at 230° uncorr. dec. and failed to depress the melting point of an authentic sample.

1,6-Dichloro-5-aminofluorenone.—This is the amine corresponding to the so-called "keto acid amide." It was prepared by substantially the same process used for the corresponding "X acid" derivative above; yield, 62%; m. p. 257° uncorr. It crystallized from alcohol in salmon-colored crystals of entirely different appearance from the isomeric derivative.

Anal. Calcd. for $C_{13}H_7Cl_2NO$: Cl, 26.90. Found: 27.02, 26.72.

5,5'-Dichlorodiphenic Acid. (Hunn's Acid) (I).⁷—This acid, previously reported by Hunn according to an entirely different procedure, was prepared by us in a manner analogous to that employed for 3,3'-dichlorodiphenic acid. This process started with commercial 4-chloro-2-aminotoluene hydrochloride ("Fast Red KB Base" of the General Dyestuffs Corporation) and passed through 4-chloro-2-acetylaminotoluene, 4-chloro-2-

(7) Hunn, *THIS JOURNAL*, **45**, 1024–1033 (1923).

acetylaminobenzoic acid, and 4-chloroanthranilic acid to the desired diphenic derivative. The original base hydrochloride with acetic anhydride in glacial acetic acid solution gave 78% yield of acetyl derivative, m. p. 130° (as recorded). Oxidation of the latter according to the procedure indicated for the 6-chloro isomer⁸ gave an 85% yield of 4-chloro-2-acetylaminobenzoic acid, m. p. 213° (recorded 214°). This was hydrolyzed by boiling two hours with 9 *N* hydrochloric acid and the nearly quantitative yield of 4-chloroanthranilic acid hydrochloride diazotized and coupled according to the method used by Hunn for a different intermediate. The melting point of the 5,5'-dichlorodiphenic acid so obtained could not be raised above 291° uncorr. although Hunn reports 297° for his product.

1,6-Dichlorofluorenone-4-carboxylic Acid (II).—The keto acid from Hunn's acid. Although Hunn reported the preparation of the anhydride corresponding to 5,5'-dichlorodiphenic acid he neglected to deal with the corresponding keto acid, which we have therefore prepared. Five grams (0.016 mole) of pure 5,5'-dichlorodiphenic acid was mixed with 12 ml. of pure concentrated sulfuric acid and the solution heated at 125 ± 1° for one hour. The dark brownish-red solution was then poured onto ice, and the precipitated acid filtered, washed free from sulfate and dried. The crude acid weighed 4.7 g. (100% theoretical) and melted 228–230°. The product was dissolved in 100 ml. warm 1 *N* sodium bicarbonate solution, filtered and reprecipitated with 6 *N* sulfuric acid. The product which first separated proved to be the difficultly soluble sodium salt of the keto acid, which after filtration was converted to the free acid by digestion with 6 *N* sulfuric acid. There was thus obtained 4.4 g. of pale yellow acid, m. p. 235–236°. After recrystallization from 40 ml. of boiling alcohol with addition of 5 ml. of water, 3.2 g. of pure keto acid, m. p. 240°, was obtained and this melting point was not raised by further recrystallization.

Anal. Calcd. for $C_{14}H_8Cl_2O_3$: Cl, 24.23. Found: 24.21, 24.23. Neut. equiv. (in alcohol) Calcd., 293.0. Found: 293.6, 293.7.

A mixture of this keto acid (m. p. 240°) with an equal amount of 1,6-dichlorofluorenone 5-carboxylic acid (m. p. 242.5°)⁸ showed a melting point depressed to 205–208°. A mixture of this keto acid (m. p. 240°) with the "Acid X" was (slightly) depressed to 235–239° and this observation was checked in a second experiment.

1,6-Dichlorofluorenone-4-carboxylic Acid Chloride.—Early attempts to prepare this acid chloride by the method employed with the keto acid from 3,3'-dichlorodiphenic acid led only to products which gave unsatisfactory analyses for chlorine. It was noted that when this keto acid was treated with thionyl chloride the immediate reaction was far more vigorous than in the two other isomeric cases. Satisfactory results were finally obtained by dissolving 1 g. (0.0034 mole) of pure 1,6-dichlorofluorenone-4-carboxylic acid in 3.7 g. (0.034 mole) of thionyl chloride and refluxing for one hour (instead of two as in the other cases). On cooling the solution 0.65 g. of clear yellow solid precipitated corresponding to 61% yield. After reprecipitation from boiling benzene with petroleum ether the melting point remained constant at 185° uncorr.

Anal. Calcd. for $C_{14}H_5Cl_3O_2$: Cl, 34.19. Found: 34.41, 34.31.

A mixture of this keto acid chloride with the corresponding derivative from "Acid X" melted at 178–180° uncorr.

1,6-Dichlorofluorenone-4-carboxylic Acid Amide.—A small sample of crude acid chloride was converted to amide by boiling with concentrated ammonium hydroxide, cooling and filtering off the insoluble solid, m. p. 268–270°. After three recrystallizations from dilute alcohol the melting point reached a constant maximum of 301° uncorr.

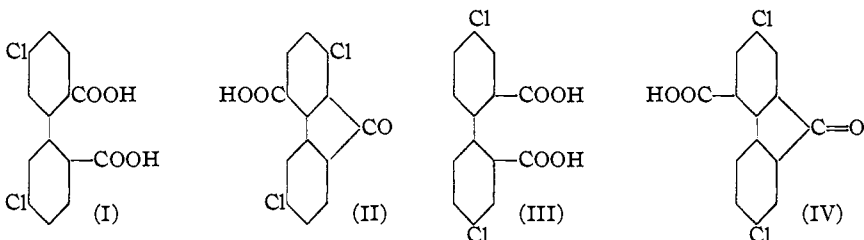
Anal. Calcd. for $C_{14}H_7Cl_2NO_2$: Cl, 24.29. Found: 24.39, 24.72.

(8) Ref. 1, p. 2562.

The melting point of a mixture of equal parts of this amide (m. p. 301°) with the "X acid" amide (m. p. 296°) was depressed to 292–294°.

Attempts to Obtain 1,6-Dichlorofluorenone from 1,6-Dichlorofluorenone-4-carboxylic Acid.—It will be recalled that when 1,6-dichlorofluorenone-5-carboxylic acid (that from 3,3'-dichlorodiphenic acid) was heated to 350° for one hour it readily lost carbon dioxide and yielded 1,6-dichlorofluorenone. When exactly the same conditions and procedure⁹ were applied to 1,6-dichlorofluorenone-4-carboxylic acid (Hunn's keto acid), however, very little carbon dioxide was evolved and after sublimation in vacuum the sublimate was found to be soluble in dilute sodium carbonate solution and to consist of unchanged keto acid. Upon raising the temperature to 400° and heating for half an hour under atmospheric pressure much charring occurred and a pure homogeneous product could not be obtained. The difference in the ease of loss of carbon dioxide from these two keto acids is notable.

4,4'-Dichlorodiphenic Acid.—This previously unreported dichlorodiphenic acid (III) was synthesized from 5-chloro-2-aminobenzoic acid (5-chloroanthranilic acid)



by the same method used for the 3,3'-isomer. The necessary substituted anthranilic acid was obtained from the interaction of sulfuryl chloride and anthranilic acid according to the directions of Eller and Klemm.¹⁰ Yields of 4,4'-dichlorodiphenic acid were about 50%. The pure product crystallizes from 50% alcohol in white needles, m. p. 264–265° uncorr. It is insoluble in water, but soluble in alcohol, ether or glacial acetic acid.

Anal. Calcd. for $C_{14}H_8Cl_2O_4$: Cl, 22.83. Found: 22.88, 23.24. Neut. equiv. Calcd., 155.5. Found: 155.2, 156.4.

As impurities from the coupling of the diazotized chloroanthranilic acid there were isolated 2,5-dichlorobenzoic acid, 2-hydroxy-5-chlorobenzoic acid and an unidentified substance of m. p. 320°.

4,4'-Dichlorodiphenic Anhydride.—The corresponding dichlorodiphenic acid was refluxed thirty minutes with excess acetic anhydride. The acid soon dissolved and on cooling the desired anhydride separated out in colorless crystals. After recrystallization from a mixture of acetic anhydride and glacial acetic acid, it was washed with dry ether and dried at 100°; m. p. 308–310° uncorr.

Anal. Calcd. for $C_{14}H_6Cl_2O_3$: Cl, 24.23. Found: 24.20, 24.36.

Upon heating above 330° for fifteen minutes, the anhydride sublimed readily with some loss of carbon dioxide and appearance of a yellow product presumably consisting of a dichlorofluorenone. This substance was not further investigated in this research.

2,7-Dichlorofluorenone-4-carboxylic Acid.—This substance (IV) has previously been reported under the designation *x,x*-dichlorofluorenone-4-carboxylic acid.¹¹ It was readily prepared by heating one gram of the 4,4'-dichlorodiphenic acid with 15 ml. of concentrated sulfuric acid at 150–170° for thirty minutes. The resulting deep reddish-

(9) Ref. 1, p. 2565.

(10) Eller and Klemm, *Ber.*, **55**, 217–224 (1922).

(11) Beilstein, 4th edition, 1st Suppl., Vol. X, p. 370.

brown solution was cooled, poured onto ice and the precipitated acid filtered off and washed. After recrystallizing from 50% alcohol it was obtained as a yellow solid, m. p. 248–249° uncorr.

Anal. Calcd. for $C_{14}H_6Cl_2O_3$: Cl, 24.23. Found: 24.18, 24.42. Neut. equiv. Calcd., 293. Found: 294, 294.

In order to examine the possible formation of isomers during this conversion, a test was made in which 0.1 g. of 4,4'-dichlorodiphenic acid was heated with 75 drops of concentrated sulfuric acid at 125° for forty-five minutes, another sample at 175° for thirty minutes and a third at 225° for fifteen minutes. The products from the first two runs were identical, melted at 248° uncorr., and failed to depress this value when mixed. At 225° or above, however, escape of carbon dioxide was noted and the crude product consisted of a mixture of the expected keto acid with 2,7-dichlorofluorenone. The former was easily separated by virtue of its solubility in sodium bicarbonate solution; the insoluble ketone which remained was recrystallized from 50% alcohol and identified by means of its melting point and color.¹² At 265–270° all of the keto acid was decomposed, the solid product obtained consisting exclusively of ketone accompanied by a small amount of its water-soluble sulfonation product.

Summary

1. When 3,3'-dichlorodiphenic acid is heated with concentrated sulfuric acid at 170° there is formed a keto carboxylic acid isomeric with, but different from, the 1,6-dichlorofluorenone-5-carboxylic acid which is quantitatively obtained at 125°.

2. This latter keto acid can be converted to the new isomeric keto acid by heating in concentrated sulfuric acid at the higher temperature.

3. Not only are these two acids definitely different but they yield different though isomeric acid chlorides and amides, and the latter degrade by the Hofmann reaction to isomeric but different amines.

4. The amino compound thus obtained from "Acid X" deaminates to yield 1,6-dichlorofluorenone, indicating that during the formation of "Acid X" both the fluorenone nucleus and the relative positions of the two halogen substituents therein are unchanged.

5. Since preliminary experiments have failed to detect the existence of a corresponding situation with the 4,4'-, 5,5'-, or 6,6'-dichlorodiphenic acids it may be that the phenomenon is associated with the 3,3'-position of the substituent groups.

6. In the course of this work the following new compounds have been reported: the new keto acid from 3,3'-dichlorodiphenic acid, its acid chloride, its amide, the corresponding amine, the "X Acid" oxime: 1,6-dichlorofluorenone-4-carboxylic acid, its acid chloride and amide; 1,6-dichloro-5-aminofluorenone; 4,4'-dichlorodiphenic acid, 4,4'-dichlorodiphenic anhydride and 2,7-dichlorofluorenone-4-carboxylic acid.

CAMBRIDGE, MASSACHUSETTS

RECEIVED JUNE 17, 1933
PUBLISHED OCTOBER 6, 1933

(12) Cf. Schmidt and Wagner, *Ann.*, **387**, 161 (1911); Courtot, *Ann. chim.*, [10] **14**, 96 (1930).