placed in a 2-liter flask with 1 liter of 2% sulfuric acid. The mixture was stirred by means of an electric motor for four hours, at the end of which time the hydroquinone had been completely converted to light yellow quinone. Because the temperature of the mixture rose to about 40° during the course of the reaction the flask was cooled in an ice mixture. The yellow solid was brought upon a filter, washed with 100 cc. of cold water and dried in a desiccator over calcium chloride yielding 90 g. of light yellow quinone melting at 110–112°. Extraction of the combined filtrate and washings with four 100-cc. portions of benzene gave an additional 14 g. of quinone. On recrystallization from ligroin (b. p. 90–120°) a 90% yield (97 g.) of pure quinone melting at 111–113° was obtained.

TABLE I

YIELDS AND MELTING POINTS OF SUBSTITUTED HYDROQUINONES

Quinone	Yield, %	M. p., °C. Crude	M. p., °C. Recryst.
Methylbenzoquinone	90	66–68	68–69
Chlorobenzoquinone	92	52–54	53.5–64
Bromobenzoquinone	94	54–55	55–56
1,4-Naphthoquinone	93	123.5–125	124.5–125

Substituted hydroquinones are oxidized similarly with equally good results when amounts of materials proportional to those above are employed. In the table are shown the percentage yields of the quinones thus obtained from the corresponding hydroquinones together with the melting points of the crude and the purified products.

Acknowledgment.—The junior author is deeply indebted to Professor N. A. Milas for valuable suggestions and assistance during the course of the present work.

Summary

Vanadium pentoxide in dilute sulfuric acid solution induces the oxidation of anthracene, hydroquinone and substituted hydroquinones with chlorates to give excellent yields of the corresponding quinones of a high degree of purity.

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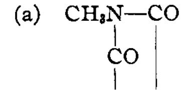
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF MOUNT HOLYOKE COLLEGE]

The Isomerization of Certain Saturated and Unsaturated Hydantoins

BY DOROTHY A. HAHN AND MARGARET K. SEIKEL

The present investigation deals with isomeric hydantoins of the types

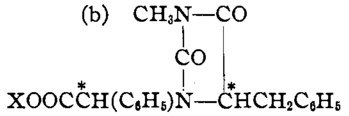
(a)



$$\begin{array}{l} \mathrm{CH_3N{-}CO} \\ \mathrm{CO} \\ \mathrm{XOOCCH(C_6H_5)N{-}C{=}CHC_6H_5} \end{array}$$

and

(b)



$$\begin{array}{l} \mathrm{CH_3N{-}CO} \\ \mathrm{CO} \\ \mathrm{XOOC\overset{*}{C}H(C_6H_5)N{-}\overset{*}{C}HCH_2C_6H_5} \end{array}$$

where X denotes H, C_2H_5, Na or Ba/2 and * denotes an asymmetric carbon. Four pairs of isomers have been isolated in each group (a) and (b). In the case of the unsaturated compounds (I to VIII) the isomers represent geometrical modifications since both VII and VIII on reduction yield the saturated acid IX.[1] The creation of a second asymmetric carbon accounts for the formation of racemic mixtures in the case of the saturated compounds (IX to XVI).

Mixtures of geometric isomers of type (a) can be resolved readily into their components through conversion to barium salts. These salts not only vary considerably in water solubility but separate from solution in well-defined crystalline forms. Transformations within each of the parallel series I, III, V, VII and II, IV, VI, VIII may be carried out quantitatively at low temperatures. Isomerization occurs at higher temperatures and notably in the presence of sodium hydroxide and hydrogen chloride. Partial and even complete hydrolysis may take place under the prolonged action of alkali. Considerable amounts of N-3-methylbenzalhydantoin and lesser amounts of N-3-methylbenzalhydantoin-N-1-phenylacetic acid along with benzaldehyde result from hydrolysis at the N-1- and C-5-positions.

Saturated hydantoins of the structure (b) may be obtained by heating compounds of the type (a) with hydrogen iodide and red phosphorus. As shown in the experimental part, ester I passes readily into the hydrate of the acid IX. The latter may be converted quantitatively into the sodium salt XIII and this into the products XI and XV. When heated with alcoholic hydrochloric acid, however, the hydrate of the acid IX yields a mixture of the esters XI and XII, which can be separated by recrystallization from alcohol.

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[1] Additional evidence was furnished by the fact that the absorption curves of the esters I and II agree closely, and are in all respects analogous to those observed in the case of other pairs of geometrical isomers having an ethylene bond in the C-5-position and substitutents in the N-1-N-3-positions. Compare Hahn and Evans, THIS JOURNAL, **50**, 810 (1928); Hahn and Dyer, *ibid.*, **52**, 2505, 2507 (1930).

The ester XII is readily transformed into the sodium salt XIV and the latter into the products X and XVI. Compounds of the structure (b) are more stable than those of type (a). However, the hydrate of the acid IX heated in barium hydroxide solution, hydrolyzes to give β-phenylalanine-N-phenylacetic acid.[2]

A comparison of the unsaturated and saturated acids derived from ethyl N-3-methyl-5-*benzalhydantoin*-N-1-phenylacetate and ethyl N-3-methyl-5-*anisalhydantoin*-N-phenyl acetate,[3] respectively, shows that the latter have been isolated in a greater number of modifications,

Experimental

Ethyl N-3-methyl-5-benzalhydantoin-N-1-phenylacetate,—I, m. p. 134–135° and II, m. p. 106.5–107.5°. Ester I was the sole product obtained when 70 g. of finely powdered methylbenzalhydantoin,[4] suspended in 280 cc. of absolute alcohol containing 8.4 g. of sodium, was refluxed for sixteen hours and then treated with 88.8 g. of ethyl phenylbromoacetate. The heating was continued for one hour when the mixture was poured into water, and the crystalline solid which separated at ice-bath temperature, washed with alcohol and water; yield 110 g. After exhaustive extraction of this material with cold chloroform, the residue consisted of 9.18 g. of methylbenzalhydantoin. To the combined extracts concentrated to small volume, 100 cc. of boiling alcohol was added. Through repeated concentration of the solution, followed by additions of alcohol, the chloroform was completely removed, when the volume was increased to 600 cc. From the chilled solution 92.2 g. of the quite pure ester (I) separated in rosets of long needles, m. p. 134–135°. When this product was dissolved in alcohol saturated with hydrogen chloride and the solution concentrated to half its volume, approximately 50% of the ester separated, m. p. 134–135°. The isomeric ester II left as a gum after the removal of the solvent would not crystallize.

The ester II was obtained in crystalline form by dissolving or suspending the acid VIII or the barium salt VI in 95% alcohol and saturating the solution with hydrogen chloride (yield 70%). Recrystallized from alcohol it separated in rosets of glistening white plates, m. p. 106.5–107.5°. The isomeric esters have the following solubilities in alcohol: (boiling) I, 1 g. in 7 cc.; II, 1 g. in less than 1 cc.; (cold) I, 1 g. in 350 cc.; II, 1 g. in 60 cc.

Anal. I. Calcd. for $C_{21}H_{20}O_4N_2$: N, 7.69. Found: N, 7.74, 7.75. II. Calcd. for $C_{21}H_{20}O_4N_2$: N, 7.69. Found: N, 7.38, 7.46.

Sodium N-3-methylbenzalhydantoin-N-1-phenylacetate.—III, m. p. 288° (dec.) and IV, m. p. 217° (dec.). A mixture of two isomeric salts was formed when 2.4 g. of sodium hydroxide dissolved in 20 cc. of water and added to 20 g. of ester I in 200 cc. of boiling 95% alcohol,[5] was refluxed for one hour. On cooling 6.0 g. of quite pure salt (III) separated. The filtrate and alcohol washings when evaporated almost to dryness and treated with 200 cc. of ether yielded the isomer (IV). The same products were obtained by adding aqueous sodium sulfate to aqueous solutions of V and VI and by neutralizing the acids VII and VIII. The salt III was recrystallized by concentrating relatively large volumes of its alcohol solutions from which it separated in fine white needles or plates. The isomer IV when dissolved in a small quantity of absolute alcohol separated in rosets of fine white needles on the addition of absolute ether.

Anal. III. Calcd. for $C_{19}H_{15}O_4N_2Na$: N, 7.82. Found: N, 7.79, 7.62. IV. Calcd. for $C_{19}H_{15}O_4N_2Na$: N, 7.82. Found: N, 7.73, 7.54.

Isomeric barium salts, V, m. p. 213–215° (dec.) and VI, m. p. 312–320° (dec.) were obtained most readily by adding aqueous barium chloride to aqueous solutions of the sodium salts III and IV. They were also prepared from the acids VII and VIII and the esters I and II. The salt V is only slightly soluble in boiling water (1 g. in 400 cc.). It was purified by concentrating large volumes of its aqueous solutions, following extractions with small quantities of boiling water, when it crystallized in tiny rosets of microscopic needles. The salt VI is readily soluble in boiling water (1 g. in 10 cc.) and on cooling separates almost completely in large glistening white plates which immediately lose water on exposure to the air forming a hard white powder. Mixtures of these two products are easily resolved.

Anal. V. Calcd. for $C_{19}H_{15}O_4N_2Ba/2{\cdot}H_2O$: H_2O, 4.27. Found: H_2O, 4.29. Calcd. for $C_{19}H_{15}O_4N_2Ba/2$: N, 6.94; Ba, 17.01. Found: N, 6.53, 6.60; Ba, 16.97, 16.89. VI. Calcd. for $C_{19}H_{15}O_4N_2Ba/2$: N, 6.94; Ba, 17.01. Found: N, 6.62, 6.54; Ba, 17.01, 16.86.

Isomeric acids VII, m. p. 186–187° and VIII, m. p. 170° were obtained by adding hydrochloric acid to aqueous solutions of the sodium salts III and IV, or the barium salts V and VI. Both tend to separate as oils from concentrated aqueous solutions but this may be prevented by the addition of acetone. Both were recrystallized from acetone–water mixtures. Both reduced to form the hydrate of the saturated acid IX when heated with hydrogen iodide and red phosphorus.

Anal. VII. Calcd. for $C_{19}H_{16}O_4N_2$: N, 8.33. Found: N, 8.24, 8.23. VIII. Calcd. for $C_{19}H_{16}O_4N_2$: N, 8.33. Found: N, 804, 8.11.

The isomeric saturated acids IX, m. p. 147–147.5° and X, m. p. 129–131°, corresponding to the structure (b), were prepared directly from their hydrates both of which melt with an evolution of water at 90–100°. The hydrate of IX is very stable but heated at 120° it loses water, passing into an oil which crystallizes in rosets of large opaque oblong prisms. Heated at 80° it melts to a glass which loses water very slowly but which when warmed with a small quantity of dry ether forms a fine anhydrous powder. The hydrate of X is unstable and loses water immediately on exposure to the air. Solutions of the anhydrous acids in dry alcohol-free ether may be distinguished by the fact that IX separates readily in large transparent oblong prisms while X separates in small transparent plates from the gum

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[2] Hahn and Litzinger, THIS JOURNAL, **54**, 4665 (1932); Litzinger and Pickett, *ibid.*, **56**, 124 (1934).

[3] Hahn and Dyer, *ibid.*, **52**, 2496 (1930).

[4] Litzinger, *ibid.*, **56**, 673 (1934).

[5] The addition of alkali was accompanied by the appearance of a deep red color which disappeared on shaking.

which remains after the solvent has almost completely evaporated.

The hydrate of IX was prepared in quantity by refluxing a mixture of 20 g. of ester I, 4.0 g. of red phosphorus and 50 cc. of hydrogen iodide (sp. gr. 1.7) on a bath kept at 105–110° for one hour. The hydrogen iodide was removed by distillation under reduced pressure followed by extractions with small quantities of boiling water. The residual gum dissolved in acetone and filtered gave a colorless solution which on addition of water deposited a homogeneous and quite pure crystalline product (yield 90%). Recrystallized from acetone–water mixtures and finally from water, the hydrate separated in small transparent prisms or plates. The same product was obtained by adding hydrochloric acid to aqueous solutions of XIII and XV in which case the addition of a small quantity of ether prevented its precipitation as an oil (yield quantitative).

The hydrate of X was prepared by adding hydrochloric acid to the aqueous solutions of XIV and XVI, the addition of ether ensuring its separation in crystalline form (yield quantitative). Recrystallized from acetone–water mixtures and finally from water, it separated in soft glistening plates.

Anal. IX. Calcd. for $C_{19}H_{18}O_4N_2 \cdot H_2O$: H_2O, 5.06. Found: 4.92, 4.89. Calcd. for $C_{19}H_{18}O_4N_2$: N, 8.28. Found: 8.12, 8.02. X. Calcd. for $C_{19}H_{18}O_4N_2$: N, 8.28. Found: 8.06, 7.98.

A mixture of isomeric esters XI, m. p. 123.5–124.5° and XII, m. p. 60–61.5° was obtained when the crude reduction product from 20 g. of ester I freed from hydrogen iodide, was dissolved in 200 cc. of 95% alcohol, filtered from red phosphorus and saturated with hydrogen chloride. Through repeated concentrations of the colorless solution, followed by additions of alcohol, the hydrogen chloride was almost completely removed when on cooling the quite pure crystalline ester (XI) separated. Small additional quantities were obtained from the filtrate and alcohol washings (yield 40–50%). After the solvent had been removed almost completely, a gum was obtained which crystallized very slowly. That this gum consisted almost exclusively of the ester XII was shown by the fact that when dissolved in alcoholic sodium hydroxide, it passed quantitatively into the salt XIV. The ester XI gave the salt XIII under the same conditions. The ester XI was formed exclusively when the salt XIII was esterified at low temperatures, while mixtures of the two esters were obtained from XIV. The ester XI is very soluble in boiling 95% alcohol (1 g. in less than 1 cc.) but less soluble in cold alcohol (1 g. in 40 cc.) from which it separates in large oblong transparent prisms. The ester XII is so soluble in cold 95% alcohol that it does not begin to crystallize until the solvent has been removed almost completely. It was purified by recrystallization from alcohol–water mixtures from which it separates in large thin glistening plates. Its purification presented experimental difficulties because of its extremely slow habit of crystallizing combined with its tendency to isomerize in solution.

Anal. XI. Calcd. for $C_{21}H_{22}O_4N_2$: N, 7.65. Found: N, 7.57, 7.53. XII. Calcd. for $C_{21}H_{22}O_4N_2$: N, 7.65. Found: N, 7.35, 7.24.

The isomeric sodium salts XIII, m. p. 156–157° and XIV, m. p. 293–295° were obtained as described from the esters XI and XII and by dissolving the acids IX and X in aqueous sodium hydroxide. They were also prepared by digesting the barium salts XV and XVI with aqueous sodium sulfate. The salt XIII was prepared in quantity when the crude reduction product from the ester I freed from hydrogen iodide was dissolved in chloroform and the colorless solution extracted with aqueous sodium hydroxide (yield quantitative). Both are very soluble in boiling water but less soluble in cold (XIII, 1 g. in 7 cc.; XIV, 1 g. in 15 cc.), XIII crystallizing in long fine soft needles and XIV in rosets of small plates.

Anal. XIII. Calcd. for $C_{19}H_{17}O_4N_2Na$: N, 7.78. Na, 6.39. Found: N, 7.58, 7.54; Na, 6.32, 6.20. XIV. Calcd. for $C_{19}H_{17}O_4N_2Na$: N, 7.78; Na, 6.39. Found: N, 7.46, 7.42; Na, 6.14, 6.00. Calcd. for $C_{19}H_{17}O_4N_2Na \cdot H_2O$: H_2O, 9.09. Found: H_2O, 9.16.

The isomeric barium salts XV, m. p. 284° (dec.) and XVI m. p. 300–307° (dec.) were obtained as white almost insoluble precipitates when aqueous barium chloride was added to aqueous solutions of XIII and XIV and when IX and X were neutralized with an equivalent of base. Both were purified by concentrating relatively large volumes of their aqueous solutions following extractions with small quantities of boiling water. Both served as additional checks in establishing relationships in the parallel series IX, XI, XIII and X, XII, XIV.

Anal. XV. Calcd. for $C_{19}H_{17}O_4N_2Ba/2$: N, 6.90; Ba, 16.87. Found: N, 6.82, 6.80; Ba, 16.86, 16.72. XVI. Calcd. for $C_{19}H_{17}O_4N_2Ba/2$: N, 6.90; Ba, 16.87. Found: N, 6.63, 6.54; Ba, 16.98, 17.08.

Summary

Hydantoins involved in the synthesis of β-phenylalanine-N-phenylacetic acid exist in both geometric and stereo-isomeric modifications. The introduction of a phenyl group into residues in the N-1-position has again been found to increase the mobility of the hydantoin molecule,

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