expected addition occurs with cyclopentadiene, anthracene or butadiene. In these cases, there is no elimination of hydrogen chloride, even at elevated temperatures.

The greater reactivity of the double bond in chloromaleic anhydride than in diethyl chloromaleate is demonstrated by the fact that under conditions favorable for rapid condensation of the anhydride with anthracene, the ethyl ester–anthracene mixture gives almost complete recovery of unchanged anthracene.

The condensation of tetraphenylcyclopentadienone and chloromaleic anhydride takes place with loss of hydrogen chloride and carbon monoxide to form tetraphenylphthalic anhydride. The usual preparation of this dye intermediate involves the condensation of maleic anhydride with tetraphenylcyclopentadienone followed by dehydrogenation using bromine or sulfur.[2] A simplification of the procedure and a material shortening of the reaction time are effected by the use of chloromaleic anhydride. The yield and purity of the product are practically unaltered.

Experimental

Condensation of Chloromaleic Anhydride with Cyclopentadiene.—Thirteen grams (0.098 mole) of chloromaleic anhydride and 6.6 g. (0.10 mole) of freshly distilled cyclopentadiene in 50 ml. of benzene were allowed to stand at room temperature overnight. The mixture was diluted with 100 ml. of petroleum ether (30–60°) and, after standing for several hours, was filtered. The yield of colorless crystalline product melting at 161° was 15 g. (75%). *Anal.* Calcd. for $C_9H_7O_3Cl$: Cl, 17.9. Found (Parr bomb): Cl, 18.0.

Condensation of Chloromaleic Anhydride with Anthracene.—Ten grams (0.075 mole) of chloromaleic anhydride and 13.5 g. (0.076 mole) of anthracene (Eastman Kodak Co.) were refluxed one hour in 50 ml. of xylene. On cooling, 13 g. (56%) of colorless crystals melting at 155° was obtained. One recrystallization from toluene raised the melting point to 157°. *Anal.* Calcd. for $C_{18}H_{11}O_3Cl$: Cl, 11.4. Found (Parr bomb): Cl, 11.3.

Condensation of Chloromaleic Anhydride with Butadiene.—Seventeen grams (0.128 mole) of chloromaleic anhydride and 9 g. (0.166 mole) of butadiene were mixed in 50 ml. of benzene. After standing stoppered for one week at room temperature, the mixture was diluted with 100 ml. of petroleum ether and, after standing overnight, was filtered. The colorless granular precipitate was recrystallized from toluene to which a few drops of glacial acetic acid had been added. The yield was 4.2 g. (16% based on chloromaleic anhydride). *Anal.* Calcd. for $C_8H_9O_4Cl$ (free acid): Cl, 17.3. Found (Parr bomb): Cl, 17.3.

Attempted Condensation of Diethyl Chloromaleate with Anthracene.—Eight grams (0.039 mole) of diethyl chloromaleate and 6 g. (0.034 mole) of anthracene in 25 ml. of xylene were refluxed five hours. On cooling, 4.5 g. of anthracene (m. p. 211–214°; mixed with original anthracene, m. p. 213°) crystallized. Concentration of the filtrate yielded an additional 0.5 g. of unchanged anthracene.

Preparation of Tetraphenylphthalic Anhydride.—Twenty grams (0.052 mole) of tetraphenylcyclopentadienone and 7.3 g. (0.055 mole) of chloromaleic anhydride (Eastman Kodak Co. practical) in 25 ml. of bromobenzene were refluxed for one hour. The mixture was cooled to 0° and filtered. The crystals of tetraphenylphthalic anhydride, which were washed first with a little cold bromobenzene, then with petroleum ether (30–60°), weighed, after drying in air, 19.5 g. (83%) and melted at 288°. The addition of 100 ml. of petroleum ether to the filtrate produced 2.7 g. of additional material melting at 278–282°.

BOYCE THOMPSON INSTITUTE FOR PLANT RESEARCH, INC.
YONKERS, NEW YORK RECEIVED MARCH 1, 1945

(2) *Org. Syntheses*, **23**, 93 (1943); Dilthey, Thewalt and Trösken, *Ber.*, **67**, 1962 (1934).

The Purification and Biological Potency of Natural *d*,γ-Tocopherol

BY LEONARD WEISLER, JAMES G. BAXTER AND MARION I. LUDWIG

The vitamin E activity of natural *d*,γ-tocopherol as measured by the Evans resorption sterility test has been observed by the Biological Department of these Laboratories to decrease as more highly purified specimens became available. This note describes the preparation and assay of the purest specimen we have yet prepared.

Early preparations were reported[1] to have about one-third the potency of α-tocopherol. In 1939 a sample was prepared from corn oil in this Laboratory and found by assay in the General Mills Laboratories to have less than one-fifteenth the potency of α-tocopherol. We attributed the low potency to decomposition of the sample since γ-tocopherol (as palmitate) was found at the same time to be one-ninth as potent as α-tocopherol. More recently a preparation from mixed vegetable oils (mainly cottonseed), after separation of α-tocopherol by chromatography,[2] had one-twelfth the potency of natural *d*,α-tocopherol[3] which appeared to support the oxidation hypothesis.

In the past year, however, C. D. Robeson and K. Meng of this Laboratory have repeatedly chromatographed supposedly pure γ-tocopherol from cottonseed oil and obtained preparations of decreased potency. Meng obtained one having as little as one-twenty-fifth the potency of α-tocopherol. This suggested that the chromatographic separations previously made might have been incomplete and that our best γ-preparation might have contained small amounts of α-tocopherol. It further suggested the possibility that pure γ-tocopherol has no biological activity as measured by the resorption sterility test. The activity of the synthetic tocopherol is still under investigation.[4]

We have recently prepared γ-tocopherol from a soybean oil distillate which contained only small amounts of α- in the mixed tocopherols, making the chromatographic separation more efficient. The details were as follows:

(1) Emerson, Emerson, Mohammad and Evans, *J. Biol. Chem.*, **122**, 99 (1937).

(2) Baxter, Robeson, Taylor and Lehman, THIS JOURNAL, **65**, 918 (1943).

(3) Joffe and Harris, *ibid.*, **65**, 925 (1943).

(4) Harris, Jensen, Joffe and Mason, *J. Biol. Chem.*, **156**, 491 (1944).

Experimental

The vitamin E fraction from soybean oil was obtained by distillation in a centrifugal molecular still and further concentrated by redistillation. The resulting fraction (42.1% tocopherol by Emmerie–Engel assay) was cooled successively at −35 and −70° in ethyl formate solution (10%) to remove sterols. The recovered oil (55% tocopherol) was purified by chromatography and converted to the palmitate in the manner previously described.[2] The γ-tocopherol palmitate, after three crystallizations from acetone, melted at 44–45°. This is the same value previously reported.[2] The ester was saponified and the free tocopherol distilled in a small pot still at 0.15–0.2 mm. pressure. Its extinction coefficient ($E^{1\%}_{1\,cm.}$ (298 mμ)) = 94.5 and that of the palmitate ($E^{1\%}_{1\,cm.}$ (286 mμ)) = 40.0 were slightly higher than those previously reported.

The γ-tocopherol so prepared was assayed in the Biological Department of this Laboratory, using the technique previously described.[3] Its potency was only one-hundredth that of *d*,α-tocopherol, supporting the aforementioned hypothesis that pure γ-tocopherol has negligible activity in curing resorptive sterility.

Recently the vitamin A sparing activity of a specimen of natural γ-tocopherol from cottonseed oil was found to be fully equal to that of α- and β-tocopherols.[5] It appears unlikely that the sparing activity of the more highly purified preparation just described will be significantly different but the point is being investigated.

(5) Hickman, Kaley and Harris, *J. Biol. Chem.*, **152**, 327 (1944).

CONTRIBUTION NO. 70 FROM THE
LABORATORIES OF DISTILLATION PRODUCTS, INC.
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ROCHESTER 13, NEW YORK RECEIVED APRIL 12, 1945

NEW COMPOUNDS

2-Phenyl-4-(4-quinolal)-5-oxazolone and 2-Phenyl-4-(4-quinolal)-5-glyoxalidone

In 1904 Erlenmeyer, Jr.,[1] suggested the general nature of the reaction between hippuric acid and benzaldehyde and the production of a glyoxalidone on treatment of the condensation product with alcoholic ammonia. Quinoline-4-aldehyde hydrate and hippuric acid condense in an analogous manner to yield 2-phenyl-4-(4-quinolal)-oxazolone-5. On treatment with ammonium hydroxide, the oxazolone yields 2-phenyl-4-(4-quinolal)-glyoxalidone-5.

2-Phenyl-4-(4-quinolal)-oxazolone-5.—A mixture of 5 g. (0.029 mole) of quinoline-4-aldehyde hydrate, 2.6 g. (0.29 mole) of fused potassium acetate, and 5.15 g. (0.29 mole) of hippuric acid was ground in a mortar and transferred to an Erlenmeyer flask. Twelve grams (0.18 mole) of acetic anhydride was added and the mixture allowed to stand for one hour. The temperature rose slowly to 70° when solution became almost complete. The mixture was cooled to room temperature, chilled in ice and filtered. The small amount of tarry matter was removed by washing with acetone. The portion of the product which dissolved in the acetone was recovered by evaporation under reduced pressure and again washed with acetone; total yield, 6.8 g. The product was purified by washing with hot water, drying and crystallization from 25 cc. of *s*-amyl alcohol. The yield consisted of fine greenish yellow needles, m. p. 171–172°. The compound is soluble in hot *n*-amyl and *s*-amyl alcohol, insoluble in dilute hydrochloric acid and dilute sodium hydroxide. It is slightly soluble in cold acetone, methyl alcohol and ethyl alcohol.

Anal. Calcd. for $C_{19}H_{12}O_2N_2$: C, 75.98; H, 4.03; N, 9.33; mol. wt., 300. Found: C, 75.56, 75.86; H, 4.26, 4.07; N, 9.25, 9.38; mol. wt., 308.

2-Phenyl-4-(quinolal)-glyoxalidone-5.—A 2-g. portion of the oxazolone was suspended in 20 cc. of 95% alcohol in a 100-cc. flask. The mixture was heated to boiling under a reflux and treated with 10 cc. of concd. ammonium hydroxide. When the yellow compound dissolved 1 g. of potassium carbonate dissolved in a little water was added and the heating continued for one hour. Small amounts of ammonium hydroxide were added from time to time. Ten cc. of 25% sodium hydroxide solution was added to the orange colored solution and the heating continued for one-half hour. The solution was cooled and made slightly acid with acetic acid. The yellow precipitate was filtered, washed with water, dried, and crystallized from *s*-amyl alcohol, washed with ether and dried; yield 1.6 g., m. p. 304–305° (dec.).

Anal. Calcd. for $C_{19}H_{13}ON_3$: C, 76.24; H, 4.38; N, 14.04. Found: C, 76.07, 76.44; H, 4.01, 4.08; N, 14.20, 14.10. Melting point of picrate was 275–277° (dec.).

The glyoxalidone treated with hydrochloric acid yielded a brilliant red compound, m. p. 308–309° (dec.).

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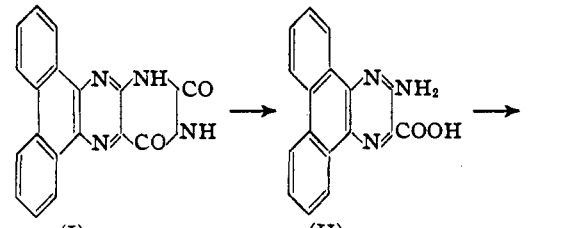
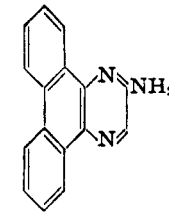
2-Amino-dibenzo[f,h]quinoxaline-3-carboxylic Acid, 2-Amino-dibenzo[f,h]quinoxaline and 2-Sulfanilamido-dibenzo[f,h]quinoxaline

By the hydrolysis of 9′,10′-phenanthrolumazine, (dibenzo[f,h]pyrimido[4,5-b]quinoxaline-11,13(10,12)-dione)[1] (I), the amino acid, 2-amino-dibenzo[f,h]quinoxaline-3-carboxylic acid (II) was obtained which could be decarboxylated readily to 2-amino-dibenzo[f,h]quinoxaline (III). The parent substance, phenanthrapyrazine, has been reported by Mazon.[2]



(I) (II)



(III)

2-Amino-dibenzo[f,h]quinoxaline-3-carboxylic Acid.—To a solution of 9 g. of sodium hydroxide in 75 cc. of water was added 9 g. of 9′,10′-phenanthrolumazine, and the mixture was held in a steel bomb at 225–235° for twenty hours. The reaction mixture was dissolved in 1000 cc. of boiling

(1) Erlenmeyer, *Ann.*, **337**, 265 (1904).

(1) Kuhn and Cook, *Ber.*, **70**, 761 (1937).

(2) Mazon, *ibid.*, **19**, 112 (1886); *ibid.*, **20**, 268 (1887); *J. Chem. Soc.*, **55**, 97 (1889).