isomeric enol form. We have been unable to convert pentaphenylacetone to its oxime and to effect reduction of the ketone by the Clemmensen method or by lithium aluminum hydride in refluxing ether. Neither have we been able to acylate the ketone with benzoyl chloride in pyridine or with a mixture of acetic anhydride and sodium acetate, indicating the presence of no appreciable amount of the enol form of the ketone.

Experimental

Pentaphenylacetone.—Potassium triphenylmethide,[6] prepared from 0.2 mole of triphenylmethane (m.p. 92.5–93°) and 0.22 mole of potassium amide in 250 ml. of ether, was carbonated[6] giving triphenylacetic acid, m.p. 262–264° (reported m.p. 263–265°)[6] in 94% yield. This acid (0.105 mole) was gently refluxed with a mixture[5] of 30 g. of phosphorus pentachloride and 90 ml. of phosphorus oxychloride giving triphenylacetyl chloride, m.p. 124–126° (reported m.p. 128–129°)[5] in 99% yield. After two recrystallizations from benzene or ligroin (b.p. 60–90°) the acid chloride melted at 126–128°; yield 89%.

To a suspension of 0.1 mole of potassium diphenylmethide in 250 ml. of dry ether,[4] immersed in a Dry Ice–acetone-bath, was added rapidly a solution of 15.3 g. (0.05 mole) of triphenylacetyl chloride (m.p. 126–128°) in 125 ml. of dry benzene. After refluxing twenty-four hours, the mixture was poured into 300 ml. of water. More ether and benzene were added and, after shaking, the aqueous-alkaline phase was separated. The ether–benzene phase was washed with water, dried over sodium sulfate and the solvents distilled. The residue was stirred with approximately 100 ml. of methanol and the solid filtered off yielding 19 g. (87%) of crude pentaphenylacetone, m.p. 174–177°. One recrystallization from a benzene–ethanol mixture gave the pure ketone, m.p. 180–181° cor. (reported m.p. 180°[2]); yield 70%.

Anal.[8] Calcd. for $C_{33}H_{26}O$: C, 90.37; H, 5.98. Found: C, 90.48, 90.75; H, 6.28, 6.17. Acidification of the aqueous alkaline phase, yielded 10% of triphenylacetic acid, m.p. 262–265°.

Tetraphenylacetone.—Potassium diphenylmethide, prepared from 0.25 mole of diphenylmethane and 0.275 mole of potassium amide in 250 ml. of ether, was carbonated[4] giving diphenylacetic acid, m.p. 146–147° (reported m.p. 147–148°)[4] in 92% yield. This acid (0.108 mole) was refluxed[9] with thionyl chloride (0.2 mole) to form diphenylacetyl chloride, m.p. 53–55° (reported m.p. 55°)[10] in 93% yield. After two recrystallizations from ligroin (b.p. 70–90°) the acid chloride melted at 54–55°; yield 61%.

To a suspension of 0.1 mole of potassium diphenylmethide in 200 ml. of ether, immersed in a Dry Ice–acetone-bath, was added rapidly a solution of 0.05 mole of diphenylacetyl chloride in 125 ml. of ether. After refluxing twelve hours, the mixture was worked up essentially as described above for pentaphenylacetone. The residue obtained on removing the solvent from the dried ether phase was stirred with 150 ml. of methanol and the remaining solid filtered off and washed with 50 ml. of methanol giving essentially pure tetraphenylacetone, m.p. 133–134° (reported m.p. 134°[7]); yield 52%. The combined methanol filtrate was steam distilled until no more diphenylmethane came over. The residue was stirred with 25 ml. of methanol giving 4.5 g. of crude tetraphenylacetone, m.p. 124–127°. This crude solid, which gave a positive hydroxamic acid test for esters,[11] was refluxed with 50 ml. of 5% sodium hydroxide solution for one hour, diluted with 200 ml. of water and the solid filtered off. In this manner there was obtained more (20%) tetraphenylacetone, m.p. 129–131° after one recrystallization from glacial acetic acid.

Acidification of the original aqueous alkaline phase yielded 19% of diphenylacetic acid, m.p. 146–147° after one recrystallization from water. Acidification of the alkaline filtrate from the refluxed mixture yielded 6% of diphenylacetic acid; this acid resulted evidently from hydrolysis of the O-acyl derivative of the ketone.

(8) Analyses by Clark Microanalytical Laboratory, Urbana, Ill.; Micro-Tech Laboratories, Skokie, Ill.

(9) Staudinger, *Ber.*, **44**, 1620 (1911).

(10) Staudinger, *ibid.*, **38**, 1737 (1905).

(11) Feigl, "Spot Tests," Elsevier Publishing Co., Inc., New York, N. Y., 1946, p. 358.

CONTRIBUTION FROM THE
DEPARTMENT OF CHEMISTRY
DUKE UNIVERSITY
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8-Methoxyhydrocoumarin

BY C. F. KOELSCH AND C. R. STEPHENS, JR.

When 8-methoxycoumarin is hydrogenated, and the product is dissolved in alkali and then precipitated with acid, there is obtained a substance, m. p. 107–108°. It has been reported[1] that this substance is 8-methoxyhydrocoumarin.

It has now been found, however, that the substance is soluble immediately in dilute sodium bicarbonate, and that its composition agrees with that calculated for **2-hydroxy-3-methoxyhydrocinnamic acid**. The compound shows no tendency to lose water when it is crystallized from ethyl acetate–ligroin or from water.

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.2; H, 6.1. Found: C, 61.5; H, 6.4.

The true **8-methoxyhydrocoumarin**, obtained in 70% yield when the hydrogenation product is isolated directly, and not dissolved in alkali, forms colorless needles from ether–ligroin, m. p. 76–77°.

Anal. Calcd. for $C_{10}H_{10}O_3$: C, 67.4; H, 5.6. Found: C, 67.7; H, 5.7.

(1) Rupp and Linck, *Arch. Pharm.*, **253**, 41 (1915).

SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA
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Effect of *p*H on the Far Ultraviolet Absorption of Tyrosine[1]

BY N. KRETCHMER AND R. TAYLOR[2]

Crammer and Neuberger[3] in their study of the shift in the absorption maximum of tyrosine from the wave length of 274 mμ in acid solutions to 295 mμ in alkaline solutions observed an increase in molecular extinction coefficients from 1290 to 2300. The usefulness of this absorption band in the analysis of intact proteins for tyrosine was mentioned. Sizer and Peacock[4] have also examined the effect of a few *p*H changes on the absorption band of tyrosine. At a *p*H of 12 there was observed an additional maximum in the tyrosine spectrum at a wave length of 240 mμ. These authors indicated that the complete ionization of the phenol group was responsible for the maximum.

In this report, a more complete study of the

(1) Aided by a grant from the Life Insurance Medical Research Fund.

(2) Chas. Pfizer and Co., Brooklyn, New York.

(3) J. L. Crammer and A. Neuberger, *Biochem. J.*, **37**, 302 (1943).

(4) I. W. Sizer and A. C. Peacock, *J. Biol. Chem.*, **171**, 767 (1947).

absorption spectra of tyrosine at shorter wave lengths and at various *p*H values has been made. Purified tyrosine was used throughout and the concentrations were verified by determination of Kjeldahl nitrogen and alpha amino nitrogen. The tyrosine was buffered in the region *p*H 5–9 with appropriate acetate, phosphate or borate buffers. Other *p*H values were obtained by adding hydrochloric acid or sodium hydroxide without the use of buffer. Values for *p*H approaching the *pK* were obtained by adding one-half equivalent of sodium hydroxide per equivalent of tyrosine. All of the ultraviolet readings were taken with the Beckman quartz spectrophotometer model DU.

As shown by the absorption curves in Fig. 1 the band at 240 mμ indicated by Sizer and Peacock[4] does not disappear in acid solutions but rather shifts to shorter wave lengths thus indicating the degree of ionization of the phenol group. A similar absorption curve was reported by Lemon[5] for vanillin.

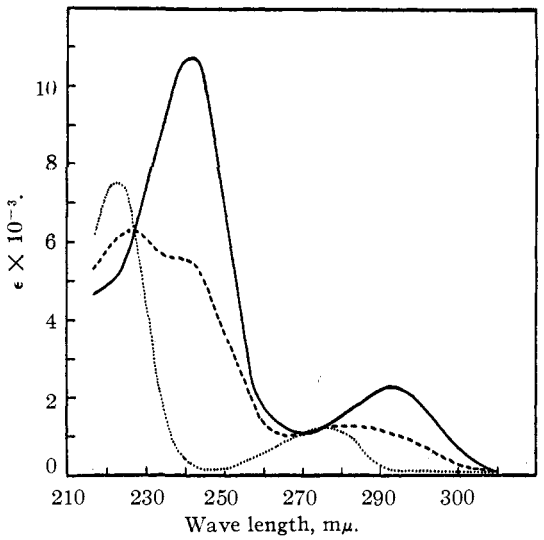

Fig. 1.—Ultraviolet absorption of tyrosine at various *p*H values: ....., *p*H < 8; - - -, *p*H = 10; ——, *p*H > 12; $\epsilon = D/cl$, c = concn. in moles/l., l = path length, D = optical density as read by Beckman spectrophotometer.

Our experimental data[6] show that the absorption curve in the "acid" range (*p*H 1 through 8) exhibits absorption maxima at 223 mμ (ϵ = 7600) and 275 mμ (ϵ = 1300). In the "alkaline" range (*p*H 12 and above) the absorption maxima are at 242 mμ (ϵ = 10,700) and 293 mμ (ϵ = 2400). At approximately the *pK* value there is an absorption band which is intermediate between that of "alkaline" solutions and "acid" solutions. The *pK* value calculated from these curves is 9.90, which is in approximate agreement with the *pK* 10.05 reported by Crammer and Neuberger.[3]

(5) H. W. Lemon, THIS JOURNAL, **69**, 2998 (1948).

(6) The authors wish to thank Miss Frances J. Cherot for her technical assistance.

The effect of "acid" and "alkaline" solutions on the far ultraviolet maximum of tyrosine is therefore essentially the same as that reported[3] for the near ultraviolet maximum in that the addition of acid shifts the maximum toward shorter wave lengths and decreases the molecular absorption coefficient. At the half ionization point for the phenolic group the observed values agree substantially with the theoretical half ionization absorption curve for tyrosine.

DEPARTMENT OF PATHOLOGY
LONG ISLAND COLLEGE OF MEDICINE
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An Improved Preparation of Gentisic Acid[1]

BY JULIUS LOWENTHAL AND J. M. PEPPER

Gentisic acid (2,5-dihydroxybenzoic acid), a metabolite of salicylic acid, has recently become of added interest because of its antirheumatic activity.[2] The reported oxidation of salicylic acid by potassium persulfate,[3] although it may be improved by a more careful control of the reaction time and temperature, gives a product which can only be purified with difficulty and great loss. A more recent publication[4] describes the preparation of gentisic acid by means of a four-step synthesis from hydroquinone diacetate in an over-all yield of 16%.

In connection with chemotherapeutic investigations attempts were made to find a more efficient synthesis for gentisic acid. Rakowski and Leppert[5] have reported the preparation of gentisic acid from 5-bromosalicylic acid by fusion with sodium hydroxide with an unspecified yield. It has now been found that this compound can also be prepared from 5-bromosalicyclic acid by heating in alkaline solution with copper powder as a catalyst.

From a series of experiments in which both temperature and time of reaction were varied, the following conditions were adopted. For the isolation of the required acid, the use of sulfur dioxide as acidifying agent, greatly facilitated the preparation of a pure product.

Experimental

The 5-bromosalicylic acid was prepared by the method of Hewitt and Kenner[6] in practically quantitative yield.

5-Bromosalicylic acid (21.7 g.) was dissolved in 500 ml. 8% sodium hydroxide solution and copper powder (20 g.) was added. The catalyst was prepared according to the method of Brewster and Groening.[7] The mixture was heated in an autoclave for one and one-half hours at 140–150°. The use of a rocking bomb did not increase the

(1) This research was conducted under a Public Health Research Grant from the Department of National Health and Welfare, Ottawa, Canada.

(2) Meyer and Ragan, *Science*, **108**, 281 (1948).

(3) Mauthner, *J. prakt. Chem.*, **156**, 150 (1940).

(4) Morris, THIS JOURNAL, **71**, 2056 (1949).

(5) Rakowski and Leppert, *Ber.*, **8**, 788 (1875).

(6) Hewitt, Kenner and Silk, *J. Chem. Soc.*, **85**, 1225 (1904).

(7) Brewster and Groening, "Organic Syntheses," Coll. Vol. II, 446 (1943).