dark red dye, crystallizing in rosets, m. p. 205–206° (Ihrig gives 206.5°), soluble in alcohol, benzene and ether, and less soluble in acetic acid (a solution of 1 g. in 75 cc., on standing in a closed container, will deposit a large amount of the crystalline solid).

*Anal.* —N=N—. Calcd.: 8.7. Found: 8.6, 8.8 (by $TiCl_3$ titration).

***dl-m*-Azophenolmandelic acid,** $HO.C_6H_4.N:N.C_6H_4.CHOH.COOH$.—This is a light yellow dye, crystallizing in plates, m. p. 119–120° (Porter and Ihrig give 119°), soluble in alcohol, benzene and in acetic acid, and slightly soluble in water.

*Anal.* Calcd.: —N=N—, 10.33. Found: 10.30, 10.26 (by $TiCl_3$ titration).

## Summary

Two asymmetric dyes, as previously prepared by Porter and Ihrig, have been synthesized.

The absorption spectra of these dyes in various solvents have been determined.

Dyeing experiments have been made with these dyes and the results from these tests have failed to confirm the previous results obtained by Porter and Ihrig. No rotation was observed in any of the solutions examined and no evidence has been obtained which would indicate the selective adsorption of one of the enantiomorphic forms of the racemic dye.

These data agree with previous data obtained by the authors and afford additional proof that the dyeing mechanism is not necessarily a chemical phenomenon.

URBANA, ILLINOIS

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY]

# THE CHEMICAL PROPERTIES OF CAPROYLRESORCINOL AND SOME OF ITS DERIVATIVES

BY D. TWISS

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Johnson and Lane,[1] and recently Leonard,[2] have announced that certain alkyl resorcinols and especially hexylresorcinol possess high bactericidal strength as compared to phenol, and that these derivatives are relatively non-toxic. Considerable interest has been developed in applying these compounds to the problem of internal antisepsis. A large number of alkyl resorcinols as well as acyl resorcinols, the products from which they are derived, have been made in the laboratories of Sharp and Dohme, Baltimore; the acyl resorcinols by condensing fatty acids with resorcinol by means of zinc chloride, the alkyl resorcinols by reducing these ketones by the method of Clemmensen,[3] which has already been applied by Johnson and Lane to the lower members of this series.

[1] Johnson and Lane, THIS JOURNAL, **43**, 348 (1921).

[2] Leonard, *J. Am. Med. Assoc.*, **83**, 2005 (1924).

[3] Clemmensen, *Ber.*, **46**, 1837 (1913).

However, at the present time little is known about the chemistry of the alkyl and acyl resorcinols, and it was therefore considered worth while to study the chemistry of one member of each series, namely, hexylresorcinol and caproylresorcinol.

As is shown in this paper, acyl resorcinols may also be obtained by condensing the esters of the fatty acids with resorcinol. For example, caproylresorcinol (resorcyl-amyl ketone) is formed when ethyl caproate and resorcinol are heated together in the presence of zinc chloride. As a condensing agent zinc chloride proved to be superior to sulfuric acid, phosphorus pentoxide and aluminum chloride or mixtures of zinc chloride and aluminum chloride. Attempts to reduce partially the caproylresorcinol in various reducing media, in order to obtain the secondary alcohol, resorcyl-amyl carbinol, did not yield positive results. Thus it was found that the ketone was not reduced at all by aluminum amalgam in acid, neutral or alkaline solution, nor by zinc powder and alcoholic sodium hydroxide. Reduction with sodium in absolute alcohol resulted in the formation of a product of high molecular weight, which dissolved in sodium hydroxide to give a dark red coloration.

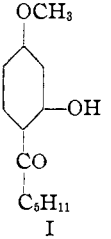
It may be desirable to point out that a large difference in chemical reactivity exists between the compounds hexylresorcinol and caproylresorcinol. There are two reasons for this: first, the difference in intensity of the steric-hindrance effect between the hexyl group in the former and the caproyl group in the latter, on the hydroxyl group in the *ortho* position to these substituents, and second, the stronger stabilizing effect of the negative caproyl group on the benzene ring as compared with that of the neutral hexyl group.

The first reason is clearly indicated by the different behavior of the two compounds on methylation. Whereas caproylresorcinol gives only the monomethyl ether, even when methylated with an excess of dimethyl sulfate or methyl iodide, hexylresorcinol gives readily mono- or dimethyl ether according to the amount of methylating agent used. Furthermore, the monomethyl ether of the ketone forms an insoluble, white, flaky sodium salt when shaken with concd. aqueous sodium hydroxide, while the monomethyl ether of the reduced compound is soluble in sodium hydroxide solution. Direct action of acetyl chloride without the addition of a solvent gives a mono-acetate in the case of the ketone and a diacetate in the case of hexylresorcinol. It was remarked that caproylresorcinol dissolves in acetyl chloride without the evolution of hydrogen chloride to give a dark red solution, and with considerable absorption of heat. The reaction begins after heating, while the color changes to yellow. When acetyl chloride is added to hexylresorcinol the evolution of hydrogen chloride begins immediately. Benzoylation according to Schotten-Baumann with *p*-nitrobenzoyl chloride gives a crystalline monobenzoate with the

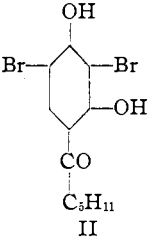
ketone. Benzoylation of hexylresorcinol with benzoyl chloride, *p*-nitrobenzoyl chloride, or 1,3-dinitrobenzoyl chloride results in the formation of non-crystallizable or tarry products.

The second reason, the stabilization of the benzene ring by the caproyl group, is clearly shown by the behavior of the two compounds on nitration or bromination. Caproylresorcinol gives a crystalline mononitro derivative, but hexylresorcinol is completely destroyed by nitric acid. Bromination of the ketone in glacial acetic acid gives a crystalline dibromo derivative, but hexylresorcinol forms an oily dibromo compound which splits off hydrogen bromide on standing. Attempts to transform this product into a stable crystalline derivative through methylation or benzoylation were not successful, as only non-crystallizable oils were obtained. An attempt to oxidize nitro- and dibromocaproylresorcinol to benzoic acid derivatives, in order to determine the positions of the bromine atoms, led to the complete alteration of the compounds. This also occurred with the monomethyl ether. The reason for this is probably that the caproyl group splits off and regenerates caproic acid, as was found to be the case with caproylresorcinol itself, and with its monomethyl ether when fused with potassium hydroxide. According to Dahse,[4] dibromoresacetophenone is more resistant toward oxidizing agents because of the stronger acidity of the acetyl group. It gives 2,4-dibromo-1,3-dihydroxybenzoic acid when oxidized with chromic acid in glacial acetic acid, and when oxidized with nitric acid dinitrobromo-dihydroxybenzoic acid is formed.

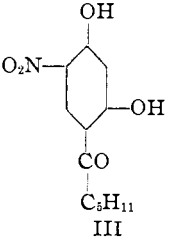
A direct proof of the constitution of the three caproylresorcinol derivatives could not be obtained. It is evident, however, that in the monomethyl ether the methyl group is attached to the hydroxyl in the *para* position to the caproyl group (Formula I).



I



II



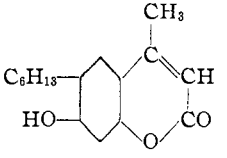
III

This must also be assumed for the monoacetate and the *p*-nitromonobenzoate. The position of the two bromine atoms in dibromocaproylresorcinol (II) must be analogous to that of the bromine atoms in dibromoresacetophenone, determined by Dahse. That is to say, one bromine atom must be *ortho* to both hydroxyl groups, and the second *ortho* to one and *para* to the other hydroxyl group. The nitro group in nitrocaproylresorcinol (III) is probably *ortho* to one and *para* to the other hydroxyl group.

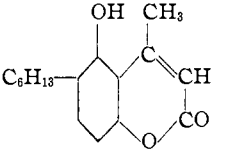
[4] Dahse, *Ber.*, **41**, 1623 (1908).

Nencki and Sieber[5] prepared a mononitro derivative of resacetophenone, but made no statements as to the position of the nitro group.

According to Tahara,[6] resacetophenone on treatment with acetic anhydride and anhydrous sodium acetate gives a small amount of a coumarin along with other products. Coumarin formation was also observed by Komarowsky and Kostanecki[7] when benzoylresorcinol was treated in a like manner. When, however, caproylresorcinol is treated with acetic anhydride and anhydrous sodium acetate, no formation of coumarin is observed. The reaction yields a thick black oil from which only a small amount of caproylresorcinol diacetate could be isolated. On treating hexylresorcinol with aceto-acetic ester in sulfuric acid solution a substituted coumarin results. Of the two possible isomers, IV and V, V must be elimi-



4-methyl-6-hexyl-7-hydroxycoumarin
IV



4-methyl-6-hexyl-5-hydroxycoumarin
V

nated as there is no evidence that the formation of the coumarin nucleus takes place between the two hydroxyl groups.

Both caproylresorcinol and hexylresorcinol show an abnormal cryoscopic behavior. A preliminary investigation showed that they form several addition compounds with benzene as well as with nitrobenzene, the exact nature of which has not yet been determined.

## Experimental Part

**Caproylresorcinol.**—Fifty-five g. of resorcinol was dissolved in 72 g. of ethyl caproate, 34 g. of zinc chloride was added and the mixture was heated and stirred for one hour at its boiling point. The reaction product was washed with water and was distilled in a vacuum. Forty-five g. of ester was recovered and 24 g. of ketone was obtained. The yield was 60% calculated on the basis of ester actually used.

*Anal.* Subs., 0.2163, 0.1440: $CO_2$, 0.5471, 0.3639; $H_2O$, 0.1493, 0.0989. Calcd. for $C_{12}H_{16}O_3$: C, 69.19; H, 7.69. Found: C, 68.98, 68.92; H, 7.55, 7.63.

The white crystals melt at 56–57°, and boil at 217–218° under 14 mm. pressure and at 343–345° under atmospheric pressure, with decomposition. Caproylresorcinol is soluble in alkali, sodium carbonate, borax and all ordinary organic solvents except petroleum ether. It also dissolves in concd. sulfuric acid from which it can be precipitated again unchanged by water, but sulfonation takes place on long standing in this solvent. The crystals become brown on long exposure to light and give a red coloration with ferric chloride in alcohol or water.

MONOMETHYL ETHER.—In 50 cc. of 20% sodium hydroxide solution was dissolved 20.8 g. of ketone, and while the solution was shaken vigorously, 20 cc. of dimethyl

[5] Nencki and Sieber, *J. prakt. Chem.*, [2] **23**, 150 (1881).

[6] Tahara, *Ber.*, **25**, 1304 (1892).

[7] Komarowsky and Kostanecki, *Ber.*, **27**, 1997 (1894).

sulfate was added in several portions. The resulting oil was dissolved in benzene, dried with calcium chloride and distilled in a vacuum. The monomethyl ether was obtained as a colorless oil, boiling at 189–192° (12–13 mm.); yield, 16 g., or 72%.

*Anal.* Subs., 0.2002: $CO_2$, 0.5158; $H_2O$, 0.1439. Calcd. for $C_{13}H_{18}O_3$: C, 70.26; H, 8.13. Found: C, 70.36; H, 7.99.

In alcoholic solution the substance gives a red coloration with ferric chloride. It is insoluble in dil. sodium hydroxide solution, and when shaken with concd. sodium hydroxide solution gives white flakes of the insoluble sodium salt. Unlike caproylresorcinol itself, the monomethyl ether shows normal cryoscopic behavior.

*Mol. wt.* Subs., 0.4483, 0.6387: benzene, 12.55; $\Delta t$, 0.899°, 1.124°. Calcd. for $C_{13}H_{18}O_3$: mol. wt., 222. Found: 221, 226.

As a by-product, a very small amount of white crystals was obtained; m. p., 35–36°. This substance gives no coloration with ferric chloride in alcoholic solution. It is probably the dimethyl ether of caproylresorcinol.

OXIME.—Ten g. of caproylresorcinol was dissolved in 50 cc. of absolute alcohol and the solution boiled for five hours with 4 g. of hydroxylamine hydrochloride and 5.8 g. of anhydrous potassium acetate. The oxime crystallized after the solution had been concentrated. Upon recrystallizing from 50% alcohol, white crystals melting at 190–191° with decomposition were obtained; yield, 7 g., or 65%.

*Anal.* Subs., 0.7243, 0.5369: cc. of 0.1 *N* $NH_3$, 30.63, 23.53. Calcd. for $C_{12}H_{17}NO_3$: N, 6.13. Found: 5.92, 6.14.

The oxime is insoluble in water and gives a dark blue-violet coloration in alcoholic solution with ferric chloride.

*p*-NITROBENZOYL ESTER.—In a solution of 8 g. of sodium hydroxide in 60 cc. of water was dissolved 20.8 g. of caproylresorcinol, and 37 g. of finely powdered *p*-nitrobenzoyl chloride was added in several portions. The mixture was shaken vigorously. The oil that separated solidified to a crystalline mass on cooling. Recrystallized from alcohol, pale yellow crystals were obtained; m. p., 89–91°; yield, 20 g., or 56%.

*Anal.* (Kjeldahl, with addition of zinc powder). Subs., 0.5795, 0.5714: cc. of 0.1 *N* $NH_3$, 17.26, 17.26. Calcd. for $C_{19}H_{19}NO_6$: N, 3.92. Found: 4.17, 4.23.

MONOACETATE.—To 20.8 g. of ketone was added 15.6 g. of acetyl chloride. The ketone gradually dissolved, and during heating on the water-bath hydrogen chloride was evolved. The reaction product was poured into water, the oil dissolved in benzene, dried with sodium sulfate and distilled in a vacuum. The colorless oil boiled at 213–215° (14 mm.); yield, 19 g., or 76%.

*Anal.* Subs., 0.2047: $CO_2$, 0.5066; $H_2O$, 0.1365. Calcd. for $C_{14}H_{18}O_4$: C, 67.16; H, 7.25. Found: C, 67.49; H, 7.41.

Dissolved in alcohol, the substance gives a red coloration with ferric chloride. No solid oxime can be obtained from the monoacetate.

DIACETATE.—A poor yield of the diacetate was obtained by boiling the ketone with anhydrous sodium acetate and acetic anhydride for several hours. Much tar was formed in the reaction. From the thick black oil thus formed the diacetate was obtained as a thick yellow oil boiling at 229–232° (13 mm., with some decomposition). Saponification with alcoholic sodium hydroxide regenerated the ketone.

MONONITRO DERIVATIVE.—Forty cc. of nitric acid (d., 1.4) was poured over 10 g. of powdered ketone. After a vigorous reaction had taken place the liquid was poured into water. The oil that separated soon solidified. After several crystallizations from alcohol the substance appeared as almost white, glistening plates; m. p., 73–74°; yield, 6.3 g., or 52%.

*Anal.* (Kjeldahl, with addition of zinc powder). Subs., 0.5456, 0.5283: cc. of 0.1 *N* $NH_3$, 21.33, 20.09. Calcd. for $C_{12}H_{15}NO_5$: N, 5.53. Found: 5.47, 5.32.

The nitro compound is slightly soluble in cold alcohol, dissolves in sodium hydroxide with development of a yellow color and gives a dark red color with ferric chloride in alcoholic solution.

DIBROMO DERIVATIVE.—Thirty-two g. of bromine (10.1 cc.) dissolved in 50 cc. of glacial acetic acid was added gradually to a solution of 20.8 g. of ketone in 50 cc. of glacial acetic acid. The reaction took place immediately with evolution of hydrogen bromide and was terminated by heating on a water-bath at 40–50° for a short time. The solution was then poured into cold water and the oil that separated solidified to a brown crystalline mass. It was pressed on a porous plate and was crystallized from 75% alcohol. Twelve g. of pale yellow needles was obtained; m. p., 102–103°; yield, 33%.

*Anal.* Subs., 0.2727: AgBr, 0.2818. Calcd. for $C_{12}H_{18}O_3Br_2$: Br, 43.68. Found: 43.98.

**Hexylresorcinol.**—Fifty g. of caproylresorcinol was reduced at boiling temperature, while the liquid was stirred vigorously, for six to eight hours with 125 g. of amalgamated zinc and 300 cc. of concd. hydrochloric acid diluted with 200 cc. of water. The resulting oil was distilled in a vacuum; yield, 35.5 g. of hexylresorcinol, or 76%.

*Anal.* Subs., 0.1301, 0.1172: $CO_2$, 0.3545, 0.3186; $H_2O$, 0.1100, 0.0976. Calcd. for $C_{12}H_{18}O_2$: C, 74.23; H, 9.28. Found: C, 74.30, 74.14; H, 9.39, 9.25.

Hexylresorcinol crystallizes from benzene in white needles and from ligroin in shining white plates; m. p., 67–68°; b. p., 198–200° at 13–14 mm. and 333–335° at atmospheric pressure. The decomposition of hexylresorcinol boiling under atmospheric pressure is less than that of the ketone. The crystals become brown on long exposure to light. The compound is soluble in all ordinary organic solvents except petroleum ether. It is, furthermore, soluble in alkali, sodium carbonate, borax and concd. sulfuric acid. From the last it may be precipitated unchanged on diluting with water. However, long standing in concd. sulfuric acid causes sulfonation. The solubility in water is 1:2000. In alcoholic solution hexylresorcinol gives a green coloration with ferric chloride.

DIMETHYL ETHER.—In 100 cc. of 20% sodium hydroxide solution was dissolved 19.4 g. of hexylresorcinol, and 40 cc. of dimethyl sulfate was added gradually. The mixture was shaken vigorously and the oil that separated was dissolved in ether, dried with calcium chloride and distilled in a vacuum. The colorless oil thus obtained boiled at 164–165° under 12 mm. pressure; yield, 15 g., or 72%.

*Anal.* Subs., 0.1048: $CO_2$, 0.2912; $H_2O$, 0.0937. Calcd. for $C_{16}H_{22}O_4$: C, 75.96; H, 9.98. Found: C, 75.78; H, 9.93.

The dimethyl ether as well as the monomethyl ether shows normal cryoscopic behavior.

*Mol. wt.* Subs., 0.2064, 0.3594: benzene, 11.88; $\Delta t$, 0.403°, 0.707°. Calcd. for $C_{14}H_{22}O_2$: mol. wt., 222. Found: 216, 214.

The dimethyl ether is insoluble in alkali and gives no coloration with ferric chloride in alcoholic solution. The monomethyl ether is obtained as an alkali-soluble, colorless oil when hexylresorcinol is treated with the calculated amount of dimethyl sulfate.

DIACETATE.—Ten g. of hexylresorcinol was mixed with 25 g. of acetyl chloride. The hexylresorcinol gradually dissolved with evolution of hydrogen chloride. The reaction was terminated by heating on a water-bath. The reaction product was poured into water, washed with sodium bicarbonate solution, dissolved in benzene, dried with sodium sulfate and distilled in a vacuum. Twelve g. of colorless oil was obtained; b. p., 198–199° (15 mm.); yield, 84%.

*Anal.* Subs., 0.2103, 0.2206: $CO_2$, 0.5338, 0.5578; $H_2O$, 0.1498, 0.1580. Calcd. for $C_{16}H_{22}O_4$: C, 69.02; H, 7.97. Found: C, 69.23, 68.96; H, 7.92, 7.96.

**Coumarin.**—In 13 g. of aceto-acetic ester was dissolved 19.4 g. of hexylresorcinol, and solution was slowly added to 400 g. of cold, 82% sulfuric acid. The mixture was left for 24 hours and then poured onto ice. The sticky substance that separated gradually solidified. It was washed several times with water and was crystallized from alcohol. Ten g. of pure substance was obtained; m. p., 165°; yield, 39%.

*Anal.* Subs., 0.1207, 0.1116: $CO_2$, 0.3254, 0.3014: $H_2O$, 0.0836, 0.0773. Calcd. for $C_{16}H_{26}O_3$: C, 73.85; H, 7.75. Found: C, 73.53, 73.65; H, 7.70, 7.60.

My thanks are due to Mr. L. C. Copeland for his assistance with several of the preparations.

## Summary

1. Caproylresorcinol was prepared by the condensation of ethyl caproate with resorcinol.

2. A comparative study was made of the behavior of caproylresorcinol and of hexylresorcinol with regard to methylation, reaction with acid chlorides, nitration, bromination and formation of coumarin.

BALTIMORE, MARYLAND

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[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY]

# META-CRESOLSULFONEPHTHALEIN, 3,6-DIMETHYLSULFONEFLUORAN AND SOME OF THEIR DERIVATIVES

BY W. R. ORNDORFF AND A. C. PURDY[1]

RECEIVED MAY 27, 1926 PUBLISHED AUGUST 5, 1926

The condensation of *m*-cresol with the anhydride or chlorides of *o*-sulfobenzoic acid was undertaken to prepare *m*-cresolsulfonephthalein. No mention of this phthalein was found in the literature. While this work was in progress, however, Cohen[2] published a preliminary note in which he mentioned *m*-cresolsulfonephthalein and tetrabromo-*m*-cresolsulfonephthalein. He stated that the former gave a color change from yellow to purple at a $P_H$ of 7.6–9.2, while the latter changed from yellow to blue-green at a $P_H$ of 4.0–5.6, but he gave no details as to the method of preparation or properties of these sulfonephthaleins, nor were any analyses given.

Investigations carried out in this Laboratory[3] have shown that the con-

[1] From a dissertation presented by A. C. Purdy to the Faculty of the Graduate School of Cornell University, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

We are indebted to the Monsanto Chemical Works, who very kindly furnished gratis the saccharin used in this investigation.

[2] Cohen, "Some New Sulfonephthalein Indicators," *Pub. Health Repts.*, **38**, 199 (1923).

[3] Orndorff and Sherwood, THIS JOURNAL, **45**, 486 (1923). Orndorff and Vose, *ibid.*, **46**, 1896 (1924). Orndorff and Cornwell, *ibid.*, **48**, 981 (1926).