Because of the insolubility of the hydrochloride of 2-sulfanilamido-4-phenylthiazole, a complete solution was not obtained during the acid hydrolysis of the corresponding acetyl derivative. The hydrochloride (m. p. 250–254°) was filtered from the hot solution and the 2-sulfanilamido-4-phenylthiazole obtained by shaking the hydrochloride with bicarbonate solution. After purification it melted at 190–191°. However, when the hydrolysis was carried out in alkali the final product melted at 205–206°. These two forms of 2-sulfanilamido-4-phenylthiazole were indistinguishable by analysis and by pharmacological tests.

**2-Sulfanilamido-2-thiazoline.**—When equal molar quantities of *p*-acetylaminobenzenesulfonyl chloride and 2-amino-2-thiazoline were condensed in pyridine according to the general procedure, the product consisted mainly of an alkali-insoluble disulfonyl derivative. When two equivalents of the sulfonyl chloride were used, an 89% yield of the disulfonyl compound was obtained. After recrystallization from alcohol and water it melted at 162–163°.

*Anal.* Calcd. for $C_{19}H_{20}O_6N_4S_3$: N, 11.30. Found: N, 11.29.

2-Sulfanilamido-2-thiazoline was obtained from the disulfonyl compound by either acid or alkaline hydrolysis and, after recrystallization from alcohol, it melted at 204–205°.

Thirteen of these sulfonamidothiazole derivatives were tested[4] against experimental streptococcal and pneumococcal infections in a standard stock strain of white mice. In the antistreptococcal tests the mice were injected intraperitoneally with one-thousand lethal doses of a virulent strain of β-hemolytic streptococci at the time of oral administration of 5 mg. of the compound. Three additional doses of 5 mg. each were administered at twenty-four, forty-eight and seventy-two hours. The antipneumococcal activity was determined by intraperitoneal injection with one-hundred lethal doses of type I pneumococci at the time of the first dose of compound. Additional doses were administered orally at seven, twenty-four, forty-eight, seventy-two and ninety-six hours. Each dose was 20 mg.

The relative chemotherapeutic effects of these compounds are recorded in Table I.

## Summary

Thirteen 2-sulfanilamido-thiazoles have been prepared and tested for their chemotherapeutic effect against experimental streptococcal and pneumococcal infections in mice.

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[4] We are indebted to Dr. Bettylee Hampil and Mr. G. W. Webster for the testing of these compounds.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

# Coumarano-coumaranes

BY JOSEPH B. NIEDERL AND RICHARD H. NAGEL[1]

With the elucidation of the structures of the crystalline condensation products of catechol and hydroquinone with α- and γ-diketones successfully accomplished,[2] the study of the structures of the condensation products of the other remaining isomeric dihydric phenol, resorcinol, and diketones was undertaken and is reported in the following.

The condensation systems studied included an aliphatic α-diketone, diacetyl, and an aromatic α-diketone, benzil. Fusions of the latter diketone with resorcinol under rather strenuous conditions have been previously reported,[3] but the structural as well as the empirical formulas advanced differ widely from the empirical and structural formulas assigned to the condensation product of benzil and resorcinol formed under the mild reaction conditions described herein. Guided by the experimental findings in mono-ketone resorcinol condensations[4] in which it was shown that resorcinol may undergo double alkylation with the formation of the corresponding alkylated phenolic coumarane it became evident that an analogous "coumarane" structure may also be assigned to the crystalline condensation products obtainable from both aliphatic and aromatic α-diketones and resorcinol.

Thus diacetyl and resorcinol yielded the 6′-hydroxy-coumarano-2′,3′:3,2-(6-hydroxy-2,3-dimethyl)-coumarane (I) of which a crystalline diacetate (Ia) and di-propionate (Ib) was prepared. Benzil and resorcinol gave the corresponding crystalline phenyl substituted coumarano-coumarane, the 6′-hydroxy-coumarano-2′,3′: 3,2-

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[1] Taken from a portion of the thesis presented by Richard H. Nagel to the Graduate School of New York University in partial fulfillment of the requirements for the degree of doctor of philosophy.

[2] J. B. Niederl and R. H. Nagel, THIS JOURNAL, **62**, 3070 (1940); **63**, 307 (1941).

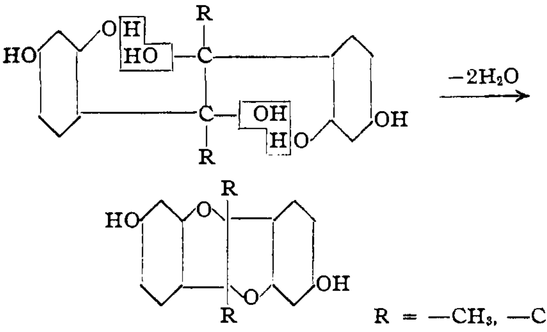
[3] J. von Liebig, *J. prakt. Chem.*, [2] **72**, 135 (1905); [2] **74**, 379 (1906); *Ann.*, **360**, 183 (1908).

[4] J. B. Niederl and V. Niederl, THIS JOURNAL, **61**, 348 (1939).

(6 - hydroxy - 2,3 - diphenyl) - coumarane (II), of which was also prepared, as in the above case, a crystalline di-acetate (IIa) and di-propionate (IIb).

In accordance with previous postulations[5] the reaction mechanism for the formation of these coumarano-coumaranes, which appear to constitute new types of compounds, might be presented as follows

$$RCOCOR + C_6H_4(OH)_2\ (m) \xrightarrow[\text{[}H_2SO_4\text{]}]{HOAc}$$



$R = —CH_3, —C_6H_5$

## Experimental

**6′ - Hydroxy - coumarano - 2′,3′: 3,2 - (6 - hydroxy - 2,3-dimethyl)-coumarane** (I).—A mixture of 1 mole of resorcinol and 0.50 mole of diacetyl was refluxed for four hours with 60 cc. of glacial acetic acid, then allowed to stand for two weeks, in which time the bulk of the material had crystallized out. The crystals were transferred to a porous tile to free them from adhering oil, and finally recrystallized several times from boiling water, m. p. 214° (uncor.).

*Anal.* Calcd. for $C_{16}H_{14}O_4$: C, 71.11; H, 5.18; mol. wt., 270. Found: C, 70.44; H, 5.64; mol. wt., 256, 273.

**Acetate** (Ia).—Two grams of the above condensation product (I) was refluxed for four hours with an excess (25 cc.) of acetic anhydride, then poured, with stirring, into a beaker of cold water and allowed to stand overnight. The crystals of the acetate were filtered off and recrystallized from 95% ethyl alcohol, m. p. 158° (uncor.).

*Anal.* Calcd. for $C_{20}H_{18}O_6$: C, 67.80; H, 5.07. Found: C, 68.54; H, 4.51.

**Propionate** (Ib).—Two grams of the above resorcinol condensate (I) and 25 cc. of propionic anhydride were refluxed for six hours, then poured into cold water and allowed to stand, with occasional shaking, until the excess reagent had hydrolyzed. The crystals formed were filtered off and recrystallized from 95% ethyl alcohol, m. p. 132° (uncor.).

*Anal.* Calcd. for $C_{22}H_{22}O_6$: C, 69.10; H, 5.76. Found: C, 69.03; H, 6.01.

**6′ - Hydroxy - coumarano - 2′,3′: 3,2 - (6 - hydroxy - 2,3-diphenyl)-coumarane** (II).—One mole of resorcinol and 0.50 mole of benzil were dissolved in 50 cc. of glacial acetic acid, the Erlenmeyer flask containing the mixture was cooled in an ice-bath, and then 25 cc. of concentrated sulfuric acid slowly added. The mixture turned dark brown and viscous, and at the end of three months had completely solidified. The mass was washed with 5% sodium carbonate solution and with cold water, then extracted with boiling chloroform. The chloroform-insoluble residue was now several times recrystallized from 50% ethyl alcohol, m. p. 254–256° (uncor.).

*Anal.* Calcd. for $C_{26}H_{18}O_4$: C, 79.19; H, 4.57; mol. wt., 394. Found: C, 79.30; H, 4.87; mol. wt., 367.

**Acetate** (IIa).—Two grams of the above condensation product (II) was refluxed for two hours with 25 cc. of acetic anhydride, then poured into ice water and let stand until the excess anhydride had hydrolyzed, then filtered and recrystallized from 95% ethyl alcohol, m. p. 182° (uncor.).

*Anal.* Calcd. for $C_{30}H_{22}O_6$: C, 75.31; H, 4.60; mol. wt., 478. Found: C, 75.37; H, 4.41; mol. wt., 480.

**Propionate** (IIb).—A mixture of 2 g. of the above condensation product (II) and 25 cc. of propionic anhydride was refluxed for four hours, then poured into cold water. The semi-solid obtained was transferred onto a porous tile, and the residue recrystallized from 95% ethyl alcohol, m. p. 113–116° (uncor.).

*Anal.* Calcd. for $C_{32}H_{26}O_6$: C, 75.88; H, 5.13. Found: C, 76.02; H, 5.35.

## Summary

The condensations of diketones with the two dihydric phenols, catechol and hydroquinone, were extended to include the third isomer, resorcinol. It was found that the nature and structures of the crystalline condensation products obtained differed with each isomer, the meta isomer yielding coumarano-coumaranes. The ortho isomer yielded indano-indanes and the para anthraquinones.

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(5) M. E. McGreal and J. B. Niederl, "Abstracts of Papers, 97th Meeting, Am. Chem. Soc.," Baltimore, Md., 1939, pp. 5–7.