TABLE V

ACETYL DERIVATIVES

				Analysis				
Anthraquinone	Yield on demethylation %	Solvent for crystallization	Color[b] and m. p. (corr.)	Formula	Subs.	G. CO_2 H_2O	Calcd. C H	Found C H
1,2,5-Trihydroxy-8-methyl	85	Acetic acid	Red 301 Decomp. at 290	$C_{15}H_{10}O_5$	0.1600	0.3913 .0558	66.65 3.73	66.72 3.90
1,2,5-Acetoxy-8-methyl	..	Alcohol	Light yellow 204–205	$C_{21}H_{16}O_8$	.1285	.2997 .0480	63.62 4.07	63.63 4.18
1,2,6,7-Tetrahydroxy[a]	69	Nitrobenzene	Orange above 330	$C_{14}H_8O_6$	.1569	.3568 .0403	61.76 2.96	62.04 2.87
1,2,6,7-Tetraacetoxy	..	Acetic acid	Light yellow 239–241	$C_{22}H_{16}O_{10}$	.1603	.3520 .0521	59.99 3.66	59.90 3.64
1,2,7-Trihydroxy-6-methyl	70	Nitrobenzene	Orange-red above 330	$C_{15}H_{10}O_5$	.1710	.4189 .0620	66.65 3.73	66.83 4.05
1,2,7-Triacetoxy-6-methyl	..	Alcohol	Light yellow 232–233	$C_{21}H_{16}O_8$	.1513	.3530 .0553	63.62 4.07	63.65 4.09

[a] Prepared by Bistrzycki, Ref. 2c.

[b] All formed needles.

Summary

1. The condensation of opianic acid with *para* substituted phenols to give substituted phthalides has been shown to be a general reaction.
2. The phthalides thus formed and the phthalides prepared by the condensation of opianic acid with *o*-cresol, guaiacol and veratrole have been reduced to the benzyl-benzoic acids.
3. The benzyl-benzoic acids have been converted to anthrones and the latter to anthraquinones.
4. A number of new anthraquinones formerly difficult of synthesis have been prepared by the general methods described.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

QUINOLINE AND THE CENTROID STRUCTURE

BY REYNOLD C. FUSON

RECEIVED APRIL 27, 1925 PUBLISHED JULY 3, 1925

In a recent article[1] the writer presented the results of an attempt to test Huggins'[2] centroid model for naphthalene. From the experimental data given there, it was concluded that naphthalene cannot have the centroid structure and, by inference at least, this structure for benzene is made doubtful. The present paper sets forth the results of a similar attempt to apply the centroid structure to quinoline and some of its derivatives.[3]

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[1] Fuson, THIS JOURNAL, **46**, 2779 (1924).

[2] Huggins, *ibid.*, **44**, 1607 (1922).

[3] The idea of using quinoline for the purpose of testing the validity of the centroid structure was suggested to the author by Dr. M. L. Huggins.

The plan of this work rests upon the proposition that bridge formation in quinoline derivatives can, according to Huggins, take place only between the 4 and 8 positions and not between the 4 and 5 positions as is required by the theory of Kekulé.[4] This is fundamental to the centroid theory. Our present problem, then, calls for the preparation of a *peri* bridge in the quinoline series and a proof of its orientation. If the bridge is found to be concerned with the 4 and 8 positions, the centroid theory will have been substantiated. On the other hand, if the bridge formation is found to occur between groups in the 4 and 5 positions, the centroid structure for quinoline will have been shown to be untenable.

So far as the writer has been able to learn, the only quinoline derivative which contains a *peri* bridge is the *lactam of 5-aminocinchoninic acid* prepared by Koenigs and Lossow[5] (Fig. 1C). They obtained this compound from cinchoninic acid by nitration and reduction of the resulting nitro compound. The amine which was first formed was found to lose water and to pass into the stable lactam.

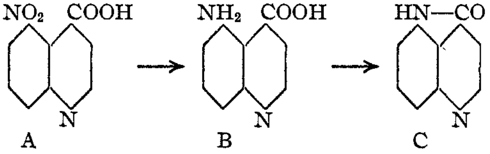

Fig. 1.

Koenigs and Lossow found that the nitrocinchoninic acid from which the amine was formed could be decomposed by heat into carbon dioxide and a nitroquinoline (m. p., 71°). That this is the 5-nitroquinoline appears from the following facts. 6-Nitroquinoline (m. p., 149–150°) and 8-nitroquinoline (m. p., 89°) are obtained by the Skraup synthesis from *p*- and *o*-nitro-aniline, respectively,[6] and hence their orientation is certain. The compound of Koenigs and Lossow must, therefore, be either the 7- or the 5-nitroquinoline. However, the fact that the nitrocinchoninic acid on reduction gives a *peri* bridge shows that the nitro group cannot, according to any existing theory, be in the 7 position. This conclusion is supported by the fact that the *m*-nitro-aniline yields by the Skraup reaction a nitroquinoline (m. p., 132–133°) unlike that of Koenigs and Lossow.[7] This would be expected to be the 7- and not the 5-compound.

As a further test of the centroid structure it seemed desirable to prepare a 4,8-disubstituted quinoline derivative containing groups in these positions which would be expected to form a bridge if the centroid structure were correct. 8-Hydroxycinchoninic acid was selected for this test.

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[4] For a detailed statement of this point see Ref. 1, p. 2780.

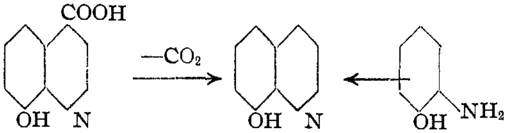
[5] Koenigs and Lossow, *Ber.*, **32,** 717 (1899).

[6] La Coste, *Ber.*, **16,** 669 (1883).

[7] Claus and Stiebel, *Ber.*, **20,** 3095 (1887).

This compound was prepared by Weidel and Cobenzl[8] from cinchoninic acid. The acid was sulfonated and the resulting sulfonic acid fused with alkali.

8-Hydroxycinchoninic acid loses carbon dioxide when heated, giving an hydroxyquinoline. This is identical with the hydroxyquinoline obtained by the Skraup synthesis from *o*-aminophenol.[9]



It follows that the hydroxyl group must occupy Position 8. All attempts to eliminate water from this acid were unsuccessful; apparently it does not form a lactone.

From these experiments it seems probable that bridge formation between groups situated in Positions 4 and 8 cannot take place; as has been indicated above, this stands in contradiction with the demands of the centroid theory. Also, the existence of the lactam of 5-aminocinchoninic acid, whose orientation seems to be beyond question, shows not only the reality of a 4,5 bridge but seems to preclude on theoretical grounds the possibility of a 4,8 bridge.[10] Moreover, these results are in complete accord with those obtained in the case of naphthalene[11] whose structure is presumably very similar to that of quinoline. It is concluded, therefore, that the centroid model does not correctly represent the quinoline molecule; and it appears probable that this structure is untenable for benzene and for aromatic nuclei in general.

Experimental Part

The preparation of 8-hydroxycinchoninic acid was carried out by the general method of Weidel and Cobenzl as indicated above, but the yields obtained by their procedure were small and uncertain so that it was found necessary to vary the method somewhat in order to make it useful for the preparation of a quantity of the acid. The revised procedure follows.

8-Sulfocinchoninic Acid.—Fifteen g. of dry cinchoninic acid was heated in a closed tube with 30 g. of fuming sulfuric acid (14% sulfur trioxide) and about 30 g. of phosphorus pentoxide. After two hours' heating at 200° the tube was cooled and opened and the melt added to about 150 cc. of water. The sulfonic acid separated after a few minutes and was filtered off and purified by recrystallization from hot water; yield, 70%. The acid shows no melting point but decomposes to a black mass above 400°.

The great stability of the compound is shown by its behavior toward potassium

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[8] Weidel and Cobenzl, *Monatsh.*, **1**, 844 (1880).

[9] Skraup, *ibid.*, **3**, 536 (1882).

[10] It is to be understood of course, that only 2-atom or 3-atom bridges are under consideration.

[11] Ref. 1, p. 2788.

cyanide. It would seem possible to replace the sulfonic group by the cyanide group by fusing the acid with potassium cyanide. The potassium salt of the acid was heated repeatedly with potassium cyanide alone and in the presence of solvents but in all of the experiments it was recovered unchanged.

8-Hydroxycinchoninic Acid.—Five g. of 8-sulfocinchoninic acid was added to a solution of 25 g. of potassium hydroxide previously dissolved in 150 cc. of water. This solution was evaporated to dryness in a silver dish. The dish was then heated in an oil-bath, the heating being continued until the residue turned a deep yellow color and test portions were found to dissolve readily in water and to give a rapid evolution of sulfur dioxide when treated with acid. This point was reached at a temperature of 280–290°. The melt was then dissolved in 300 cc. of water and dil. sulfuric acid added until the 8-hydroxycinchoninic acid was set free. The pure acid was obtained by repeated recrystallization from hot water; it melts at 258–259°. This method gave good yields and a product which was apparently somewhat purer than that obtained by Weidel and Cobenzl who give 254–256° as the melting point of their acid.

Various methods were used in an attempt to dehydrate the acid, the ones employed being those which have been found to cause condensation of similar groups in other compounds of this sort, notably in the naphthalene series. It was subjected to temperatures near its melting point for long periods of time but remained unchanged. It was observed in early experiments that after a sample had been melted repeatedly its melting point was somewhat lowered and at the same time the substance became dark colored, apparently from decomposition. Later work on very pure materials, however, showed that so long as the acid was not exposed to temperatures very far above its melting point it could be melted repeatedly without change. The compound was boiled with a number of solvents such as water, alcohol and ether; boiling acids were also tried. These methods proving futile, more drastic ones were used. The material was heated for hours with strong dehydrating agents such as phosphorus pentoxide and fuming sulfuric acid. In every case the acid was recovered unchanged.

The writer wishes to take this opportunity to express his indebtedness to Professor Gerald E. K. Branch for helpful suggestions and criticisms.

Summary

1. Attention has been called to the existence of a quinoline compound which contains a *peri* bridge, namely, the lactam of 5-aminocinchoninic acid. The orientation assigned to this compound has been shown to be correct.

2. 8-Hydroxycinchoninic acid has been prepared by the method of Weidel and Cobenzl and its orientation verified. The method of preparation has been improved and the acid produced in a higher state of purity and in better yields.

3. Attempts have been made to dehydrate this acid and cause it to form a 4,8 bridge but without success.

4. From these data it has been concluded that quinoline cannot have the centroid structure proposed by Huggins. From this it has been inferred that the centroid structure is untenable for benzene and aromatic nuclei in general.

Harvard University
Cambridge 38, Massachusetts