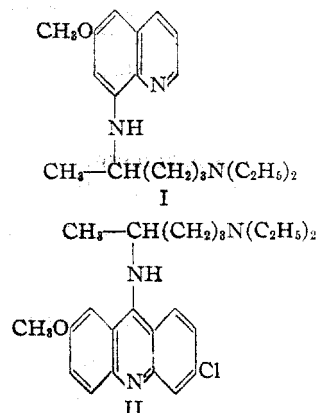


[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

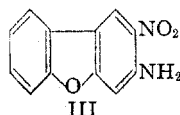
## Substituted Aminobenzofuroquinolines

BY ROGER ADAMS, J. H. CLARK,<sup>1</sup> NATHAN KORNBLUM AND HANS WOLFF

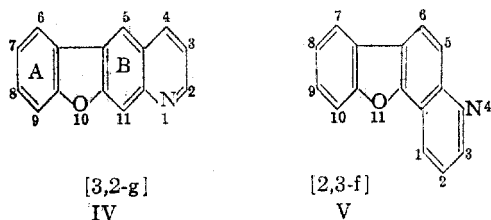
The intensive search in many laboratories to find an anti-malarial with more favorable properties than plasmochin (I) or atabrine (II) has led us to a study of certain aminobenzofuroquinolines. These compounds resemble plasmochin in their basic structure.



The failure of Kirkpatrick and Parker<sup>2</sup> to isolate a nitroquinoline from a Skraup reaction involving 2-nitro-3-aminodibenzofuran (III) made



it appear advisable to prepare the desired nitrobenzofuroquinolines by nitration of the previously described<sup>2,3</sup> benzofuroquinolines, IV and V.

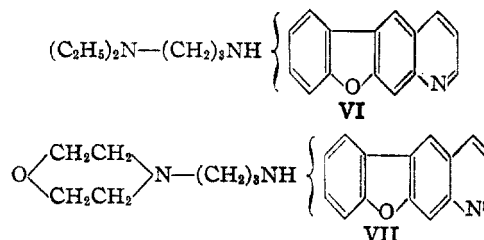


These latter compounds were synthesized following the method of Mosettig and Robinson,<sup>3</sup> and the isomers were isolated taking advantage of the contrasting solubility relationships of the free bases and their sulfates.

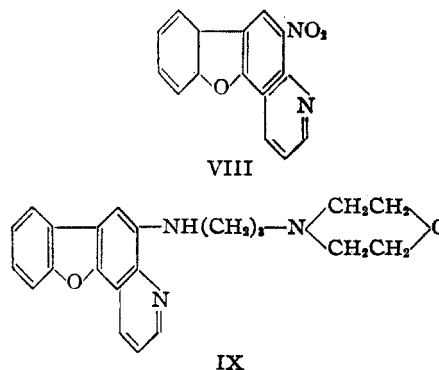
The pure quinolines were nitrated by treating the crystalline material with a large excess of fuming nitric acid followed by immediate dilution of the reaction mixture with water. A single isomer was isolated readily from the compound IV but some difficulty was encountered with com-

pound V. In this latter case a mixture resulted from which two pure isomeric mononitrobenzofuroquinolines were finally isolated. It has not been possible, as yet, to determine the position at which nitration occurred in any of the three cases.

Owing to the tediousness of separation of the isomeric mononitro compounds from V, only the derivative of IV was studied from the standpoint of obtaining a substance with antimalarial activity. The corresponding amine was condensed with 3-chloro-N,N-diethylpropylamine hydrochloride to give compound VI and with N-(3-chloropropyl)-morpholine hydrochloride to give compound VII. Neither of these substances showed antimalarial activity.



Further efforts were turned toward the synthesis of compounds of unquestionable structure in which the side chain would be attached to the quinoline portion of the benzofuroquinoline nucleus. Contrary to the experience of Kirkpatrick and Parker, it was found possible to prepare 5-nitrobenzofuro[2,3-f]quinoline (VIII) from 2-nitro-3-aminodibenzofuran (III). This compound was reduced and the morpholinylpropyl group introduced to give compound IX. This also showed no antimalarial properties.



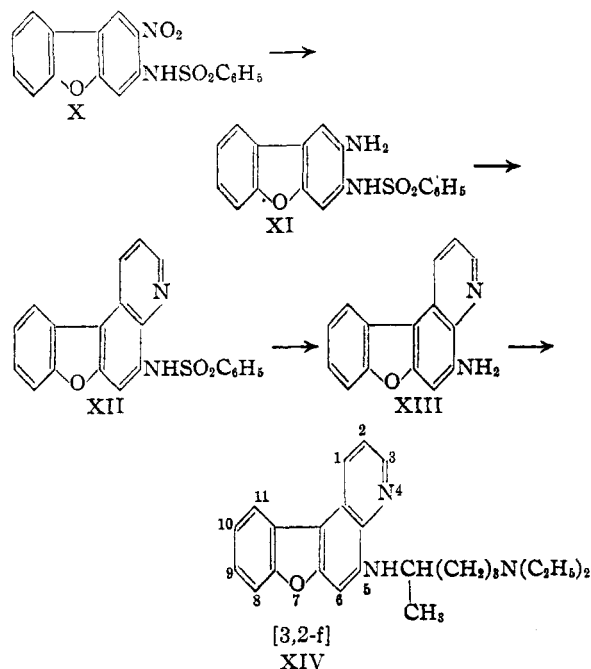
An isomer of the amine from which this derivative IX was obtained is shown in XIII. This resembles much more closely the base from which the plasmochin molecule is derived. Its synthesis was accomplished from the 3-benzenesulfon-

(1) An abstract of a thesis submitted in partial fulfillment for the degree of Doctor of Philosophy in Chemistry.

(2) Kirkpatrick and Parker, *THIS JOURNAL*, **57**, 1123 (1935).

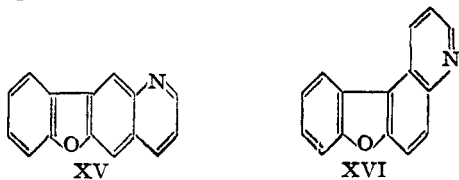
(3) Mosettig and Robinson, *ibid.*, **57**, 903 (1935).

amido-2-nitrodibenzofuran (X) which was prepared by the action of benzenesulfonyl chloride on compound III. In this case the dibenzenesulfonamido derivative was formed very easily and, therefore, it was preferable to prepare compound X by nitration of 3-benzenesulfonamidodibenzofuran. Upon reduction the corresponding amine



(XI) resulted; by means of a Skraup synthesis this yielded the benzofuroquinoline derivative (XII). Hydrolysis gave the aminobenzofuroquinoline (XIII). Alkylation of compound XIII proved to be unusually difficult and an absolutely pure product (XIV) was not isolated.

From a Skraup synthesis on 2-aminodibenzofuran, Kirkpatrick and Parker<sup>2</sup> have obtained two isomeric benzofuroquinolines, presumably having the structures of XV and XVI. These two products, to which individual structures were not assigned, melted at 185–186° and 160.5–161.5°. It was anticipated that replacement of the amino group in compound XIII by hydrogen would give a product having the structure XVI and identical in its properties with one of those obtained by Kirkpatrick and Parker. The benzofuroquinoline obtained, however, melted at 82–83.5°. The method used in the preparation of this compound would seem to leave no doubt as to its structure; no explanation for this discrepancy presents itself.



By diazotization and treatment with sodium bromide, the two aminobenzofuro[2,3-f]quino-

lines were converted to the corresponding bromo derivatives.

### Experimental

**Benzofuro[3,2-g]quinoline (linear compound) (IV) and Benzofuro[2,3-f]quinoline (angular compound) (V).**—The procedure of Mosettig and Robinson<sup>3</sup> was used with slight variations. It was found advantageous to use crude 3-aminodibenzofuran sulfate in the quinoline synthesis since the amine is isolated more readily in this form.<sup>4</sup>

The crude reaction product was distilled without any attempt at fractionation, b. p. around 200° (1 mm.); yield, 74%. The two isomers, linear and angular, were separated by the following procedure. Crystallization of 59 g. of the distilled material from 300 cc. of 95% ethanol gave 13 g. of crude linear polymer, m. p. 160–167°. The mother liquor was diluted to 600 cc. with 95% ethanol, and 15 cc. of concentrated sulfuric acid in 50 cc. of ethanol was added. At the end of fifteen minutes a heavy precipitate had formed. This was collected on a filter, washed with hot ethanol to remove the more soluble linear isomer and dissolved in water. The base, freed with concentrated aqueous ammonia, separated as an oil but solidified on standing. It was collected on a filter, dissolved in boiling petroleum ether (b. p. 60–110°), filtered hot and allowed to crystallize. In this way 10 g. of crude angular isomer was obtained, m. p. 100–106°.

The mother liquor from the sulfate of the angular isomer was evaporated to a thick sirup, treated with aqueous ammonia to free the base, diluted with water to a volume of 600 cc. and digested on a hot plate for thirty minutes. The solid was collected on a filter and recrystallized from ethanol to obtain more of the linear isomer. Repetition of this whole procedure four times gave 24.4 g. of angular isomer, m. p. 100–106°, and 24 g. of linear isomer, m. p. 160–166°. Residual material melting below 95° was discarded.

Two further crystallizations of the linear isomer from ethanol gave 21 g. (26%) of material, m. p. 168–169° (cor.), a value in agreement with that previously reported.<sup>2,3</sup>

Three crystallizations of the sulfate of the angular isomer from ethanol were necessary to give 19.5 g. (24%) of free base, m. p. 106–106.5° (cor.) which agrees with the value reported by Mosettig and Robinson.<sup>3</sup>

**Nitrobenzofuro[3,2-g]quinoline.**—To 9.6 g. of benzofuro[3,2-g]quinoline (IV) was added 30 cc. of fuming nitric acid (sp. gr. 1.50). A vigorous reaction with evolution of oxides of nitrogen ensued and the solid dissolved within thirty seconds. The reaction mixture was diluted immediately with 400 cc. of water and the product, a solid pasty mass, filtered and digested on a steam-bath with excess aqueous ammonia. The precipitate was filtered, sucked as dry as possible, suspended in 800 cc. of xylene, boiled until all the water was removed and filtered hot through a fluted filter. Upon cooling, a cream-colored crystalline product separated which was essentially pure, m. p. 267–268° (cor.); yield, 9.6 g. (84%).

*Anal.* Calcd. for  $C_{15}H_8N_2O_3$ : N, 10.60. Found: N, 10.68.

**Aminobenzofuro[3,2-g]quinoline.**—A suspension of 5 g. of nitrobenzofuro[3,2-g]quinoline in 150 cc. of 95% ethanol was reduced with 3 g. of Raney nickel and hydrogen at 2–3 atmospheres pressure. At the end of about sixteen hours the reduction was complete. The reaction mixture was heated to boiling, filtered from catalyst and then cooled. Recrystallization from ethanol gave yellow needles, m. p. 236.5–237° (cor.); yield, 3.9 g. (88%).

*Anal.* Calcd. for  $C_{15}H_{10}N_2O$ : N, 11.96. Found: N, 12.19.

**(3-Diethylaminopropylamino)-benzofuro[3,2-g]quinoline (VI).**—A mixture of 16 g. of aminobenzofuro[3,2-g]quinoline and 30 g. of 3-chloro-N,N-diethylpropylamine hydrochloride in 75 cc. of pure *n*-butanol was heated in an oil-bath at 140° with stirring for sixty hours. After evaporation of the ethanol an excess of 10% aqueous sodium

(4) Borsche and Bothe, *Ber.*, **41**, 1940 (1908).

hydroxide was added to liberate the base. It was extracted with benzene. The product, a viscous yellow oil, was obtained by high vacuum (0.02 mm.) distillation; bath temperature, 250–260°; yield 11.5 g. (48%).

*Anal.* Calcd. for  $C_{22}H_{26}N_2O$ : C, 76.05; H, 7.25; N, 12.09. Found: C, 76.16; H, 7.26; N, 11.87.

The product could not be crystallized and no crystalline salts were found. A large excess of 3-chloro-N,N-diethylpropylamine hydrochloride is necessary if a pure product is to be obtained.

**[3-(4-Morpholinyl)-propylamino]-benzofuro[3,2-g]quinoline (VII).**—A mixture of 15 g. of aminobenzofuro[3,2-g]quinoline, 20 g. of N-(3-chloropropyl)-morpholine hydrochloride and 100 cc. of pure *n*-butanol was heated in an oil-bath at 140–150° with stirring for fifteen hours. The butanol was distilled and the residual gummy solid washed with three 50-cc. portions of absolute ethanol-ethyl acetate mixture (1:2). The solid was recrystallized once from glacial acetic acid to give a pale pink powder which appeared to be a mixture of the hydrochlorides of the base. Upon dissolving in water and treating with excess of aqueous ammonia, a yellow solid separated. It was purified by recrystallization from petroleum ether (b. p. 60–110°); yellow needles, m. p. 120° (cor.); yield, 7.5 g. (32%).

*Anal.* Calcd. for  $C_{32}H_{32}N_2O_2$ : C, 73.10; H, 6.42; N, 11.63. Found: C, 72.96; H, 6.24; N, 11.81.

**Nitration of Benzofuro[2,3-f]quinoline.**—The same procedure was used as in the nitration of the isomer. The crude reaction product from 9 g. of starting material was treated with aqueous ammonia, filtered, sucked dry, treated with 400 cc. of xylene, boiled until all the water was removed, treated with Norite and filtered hot. Evaporation of the solvent gave 9.5 g. of yellow solid. This material was suspended in about 200 cc. of ethanol, the mixture boiled for ten minutes and filtered hot through a preheated fluted filter. The ethanol-insoluble material remaining on the filter amounted to 6 g. and the ethanol-soluble 3.5 g. No pure compounds could be obtained from the soluble portion.

The ethanol-insoluble product was recrystallized six to eight times from glacial acetic acid. Cream-colored needles were obtained thus, m. p. 297–298° (cor.).

*Anal.* Calcd. for  $C_{18}H_{18}N_2O_3$ : C, 68.18; H, 3.05; N, 10.60. Found: C, 68.07; H, 3.28; N, 10.66.

The residues from the glacial acetic acid filtrate after removal of the solvent were extracted thoroughly four times with cold 5% aqueous hydrochloric acid to remove any isomer, m. p. 297–298°, which was present. They were then treated with aqueous ammonia and recrystallized from toluene; yellow needles, m. p. 282° (cor.).

*Anal.* Calcd. for  $C_{18}H_{18}N_2O_3$ : C, 68.18; H, 3.05; N, 10.60. Found: C, 68.13; H, 3.02; N, 10.48.

**Aminobenzofuro[2,3-f]quinolines.**—A suspension of 15 g. of pure nitrobenzofuro[2,3-f]quinoline, m. p. 297–298°, in 150 cc. of ethanol, was reduced with hydrogen at 3 atmospheres pressure using 3 g. of Raney nickel catalyst. The product was crystallized from toluene; yellow needles, m. p. 200° (cor.); yield, 10 g. (75%).

*Anal.* Calcd. for  $C_{18}H_{16}N_2O$ : C, 76.91; H, 4.30; N, 11.96. Found: C, 77.25; H, 4.54; N, 12.16.

Reduction of the nitro isomer, m. p. 282°, gave the corresponding amine. It was purified from benzene; yellow platelets, m. p. 233° (cor.).

*Anal.* Calcd. for  $C_{18}H_{16}N_2O$ : N, 11.96. Found: N, 12.15.

**Bromobenzofuro[2,3-f]quinoline from Aminobenzofuro[2,3-f]quinoline, m. p. 200°.**—To a boiling suspension of cuprous bromide prepared from 6.3 g. of copper sulfate, 20 g. of copper turnings, and 15.4 g. of sodium bromide according to the method given in "Organic Syntheses,"<sup>18</sup> was added the diazonium bromide prepared from 2 g. of aminobenzofuro[2,3-f]quinoline, m. p. 200°, 15 cc. of 42% hydrobromic acid, 35 cc. of water, and 0.65 g. of sodium nitrite.

The mixture was refluxed for thirty minutes, cooled, and 100 cc. of benzene added, followed by an excess of aqueous ammonia. The aqueous layer was removed and the benzene solution washed three times with water. The washings were discarded.

The benzene layer was then extracted four times with an excess of dilute hydrochloric acid. The aqueous layer contained a pink solid in suspension. This aqueous suspension was removed and heated to drive off traces of benzene and then made alkaline with aqueous ammonia. A yellow solid separated which was dissolved in toluene, treated with Norite and concentrated to give white needles, m. p. 180–182° (cor.); yield, 1.28 g.

*Anal.* Calcd. for  $C_{18}H_{16}BrNO$ : C, 60.43; H, 2.70; N, 4.70. Found: C, 60.45; H, 2.74; N, 5.00.

**Bromobenzofuro[2,3-f]quinoline from Aminobenzofuro[2,3-f]quinoline, m. p. 233°.**—This compound, prepared from 0.45 g. of aminobenzofuro[2,3-f]quinoline, m. p. 233°, by the method previously described, formed white platelets from a mixture of ethanol and benzene, m. p. 204° (cor.); yield, 0.05 g.

*Anal.* Calcd. for  $C_{18}H_{16}BrNO$ : N, 4.70; Br, 26.81. Found: N, 4.52, Br, 26.20.

**3-Acetaminodibenzofuran.**—The procedure of Borsche and Schacke<sup>9</sup> was used, modified merely in doubling the amount of sodium acetate and refluxing three hours instead of one; yield 92% of a product, m. p. 183° (cor.). Borsche reports 178°.

**2-Nitro-3-acetaminodibenzofuran.**—The procedure was based on that described by Gilman, Brown, Bywater and Kirkpatrick.<sup>7</sup> To a solution of 56 g. of 3-acetaminodibenzofuran in 300 cc. of glacial acetic acid was gradually added with cooling and stirring 40 g. of fuming nitric acid (sp. gr. 1.50). Golden yellow platelets appeared almost at once and increased in amount until at the end of twenty minutes, the mixture had set to a thick pasty mass. The product was filtered and sucked as dry as possible; yellow platelets from glacial acetic acid, m. p. 205° (cor.); yield 49 g. (73%). Gilman, *et al.*, report 196°.

Dilution of the filtrate from the reaction mixture caused the precipitation of a dirty yellow solid. It was composed of a little impure starting material and a compound which crystallized from boiling xylene in the form of silky yellow needles, m. p. 261–262° (cor.). This compound was not investigated further.

**2-Nitro-3-aminodibenzofuran.**—The method of Borsche and Schacke<sup>7</sup> was employed. The product was purified from xylene; orange needles, m. p. 232–233° (cor.); yield, 86%. Borsche reports m. p. 222°.

**5-Nitrobenzofuro[2,3-f]quinoline (VIII).**—To a mixture of 32 g. of 2-nitro-3-aminodibenzofuran and 21 g. of arsenic acid ( $H_3AsO_4 \cdot \frac{1}{2}H_2O$ ) was added 32 g. of dry glycerol followed by 41 g. of concentrated sulfuric acid in small portions. The mixture was heated in an oil-bath at 130–140° for five hours and then poured over cracked ice. The product, a black tar, was extracted three times with 600-cc. portions of 10% sulfuric acid, then with boiling xylene. From the xylene solution were obtained yellow crystals which were pure after one recrystallization from the same solvent, m. p. 206–207° (cor.); yield, 9 g. (24%).

*Anal.* Calcd. for  $C_{18}H_{16}N_2O_3$ : C, 68.18; H, 3.05; N, 10.60. Found: C, 68.10; H, 3.09; N, 10.55.

**5-Aminobenzofuro[2,3-f]quinoline.**—The product was formed by reducing 5.7 g. of the nitro compound in ethanol at 50° and 3 atmospheres pressure, with Raney nickel and a pinch of platinum oxide as catalyst. The solvent was evaporated, the residue dissolved in hot petroleum ether (b. p. 60–110°) and the solution filtered hot to remove dark brown insoluble impurities; yellow needles, m. p. 197–198° (cor.); yield, 4.4 g. (87%).

*Anal.* Calcd. for  $C_{18}H_{16}N_2O$ : C, 76.91; H, 4.30; N, 11.96. Found: C, 77.28; H, 4.30; N, 11.67.

(6) Borsche and Schacke, *Ber.*, **56**, 2498 (1923).

(7) Gilman, Brown, Bywater and Kirkpatrick, *THIS JOURNAL*, **56**, 2473 (1934).

(8) "Organic Syntheses," Coll. Vol. I, p. 131.

**5-[3-(4-Morpholinyl)-propylamino]-benzofuro[2,3-f]quinoline (IX).**—A suspension of 13 g. of 5-aminobenzofuro[2,3-f]quinoline and 30 g. of N-(3-chloropropyl)-morpholine hydrochloride in 100 cc. of *n*-butanol was stirred at 145° for twenty-four hours. At this point 5 cc. of 3-(4-morpholinyl)-1-propanol was added to free any of the 5-aminobenzofuro[2,3-f]quinoline which may have been in the form of hydrochloride. The reaction mixture became much less viscous. Heating was continued for twenty-four hours more and a part of the butanol then removed on the steam cone under an air jet.

To the resulting brick red, pasty product was added a mixture of 60 cc. of methyl acetate and 30 cc. of methanol. Most of the product dissolved leaving in suspension fine, cream-colored needles which were found to be the hydrochloride of 5-aminobenzofuro[2,3-f]quinoline. The recovered material amounted to 2 g. The solvent was evaporated and a thick brown oil resulted. This was made alkaline with aqueous sodium hydroxide and extracted with benzene. The solvent was evaporated and the product distilled at a pressure of 0.03 mm. About 2 cc. of an oil distilling at 80–100° was not investigated further. It was probably a polymer of chloropropylmorpholine. An additional 0.5 g. of unchanged 5-aminobenzofuro[2,3-f]quinoline distilled at about 200°. It was necessary to stop the distillation and remove this solid from the sidearm of the distilling flask.

The desired product distilled as an orange-yellow, semi-solid resin, b. p. 238–240° (0.03 mm.) (bath temperature 265–275°).

*Anal.* Calcd. for  $C_{22}H_{23}N_3O_2$ : C, 73.10; H, 6.42. Found: C, 72.98; H, 6.75.

**3-Benzenesulfonamidodibenzofuran.**—A mixture consisting of 2 g. of 3-aminodibenzofuran, 25 cc. of 10% aqueous sodium hydroxide and 2.5 cc. of benzenesulfonyl chloride was shaken vigorously for five to ten minutes. The white solid was filtered and sucked as dry as possible.

The sodium salt thus obtained was added to 800 cc. of boiling water and filtered. The solution was then acidified with hydrochloric acid and digested on the steam-bath for one-half hour. The precipitate was dissolved in 95% ethanol, treated with Norite, concentrated and cooled. The white needles which separated were recrystallized from aqueous ethanol, m. p. 162–163° (cor.). The product is soluble in hot chloroform and hot glacial acetic acid.

*Anal.* Calcd. for  $C_{18}H_{15}NO_3S$ : C, 66.87; H, 4.02; N, 4.33. Found: C, 66.52; H, 4.14; N, 4.07.

**2-Nitro-3-benzenesulfonamidodibenzofuran (X).**—A. (Used for preparation.) A solution of 0.5 g. of 3-benzenesulfonamidodibenzofuran in 15 cc. of hot glacial acetic acid was cooled to 18° and while stirring and cooling, 0.17 cc. of nitric acid (sp. gr. 1.5) was added dropwise. The mixture was maintained at 18°. After a few minutes the nitro compound started to precipitate and was filtered with suction after ten minutes of standing. The yellow solid was sucked as dry as possible and then recrystallized from pyridine; yellow needles, m. p. 226–227° (cor.); yield, 0.26 g.

*Anal.* Calcd. for  $C_{18}H_{12}N_2O_6S$ : C, 58.69; H, 3.26. Found: C, 58.68; H, 3.19.

Hydrolysis of this compound was accomplished by refluxing for sixty hours 0.085 g. of 2-nitro-3-benzenesulfonamidodibenzofuran with 250 cc. of 25% hydrochloric acid. The mixture was filtered hot and the filtrate made alkaline. The precipitate was dried and recrystallized from xylene; orange needles, m. p. 232–233° (cor.). A mixed melting point with an authentic sample of 2-nitro-3-aminodibenzofuran showed no depression.

**B.**—A solution of 2.25 g. of 2-nitro-3-aminodibenzofuran in 100 cc. of pyridine was treated with 1.5 cc. of benzenesulfonyl chloride and immediately refluxed for seven and one-half hours. By addition of water a precipitate formed (1.85 g.). To remove any unchanged amine the crude material was dissolved in nitrobenzene and dry hydrogen chloride passed in. A small amount of precipitate was filtered and discarded. The nitrobenzene was distilled off and the residue purified from pyridine; orange crystals, m. p. 226–227° (cor.).

*Anal.* Calcd. for  $C_{18}H_{12}N_2O_6S$ : C, 58.69; H, 3.26. Found: C, 58.70; H, 3.29.

This product was identical with that obtained by nitrating 2-benzenesulfonamidodibenzofuran. It was always difficult to obtain it in a pure state by use of procedure B.

In several experiments the preparation B just described was not duplicated. Thus, in some cases, upon dilution of the reaction mixture, a yellow solid separated which was purified twice from xylene followed by two purifications from pyridine; yellow crystals, m. p. 263–265° (cor.) with decomposition and evolution of gas. It proved by analysis to be a disulfonamido derivative.

*Anal.* Calcd. for  $C_{24}H_{16}N_2O_7S_2$ : C, 56.69; H, 3.15; N, 5.51. Found: C, 56.83; H, 3.21; N, 5.52.

**2-Amino-3-benzenesulfonamidodibenzofuran (XI).**—To a suspension of 7.2 g. of 2-nitro-3-benzenesulfonamidodibenzofuran in 150 cc. of 95% ethanol, 0.05 g. of platinum oxide catalyst was added and the reduction carried out at 2–3 atmospheres pressure. The color of the material changed from deep yellow into a very light gray. The suspended amine and catalyst were refluxed with toluene. The resulting solution was filtered from the catalyst and the toluene cooled, giving asbestos-like needles; m. p. 227–228° (cor.); yield, 5.1 g.

*Anal.* Calcd. for  $C_{18}H_{14}N_2O_2S$ : C, 63.89; H, 4.18. Found: C, 63.94; H, 4.10.

**5-Benzenesulfonamidobenzofuro[3,2-f]quinoline (XII).**—To 60 g. of the 2-amino-3-benzenesulfonamidodibenzofuran, 68 g. of nitrobenzene and 73.1 g. of freshly distilled glycerol, 41.6 g. of concentrated sulfuric acid was added and the mixture was heated on a steam cone for one hour. Heating was continued in an oil-bath, the temperature of which was gradually raised to 145–150° and maintained at that temperature for five hours. The excess of nitrobenzene was separated by steam distillation and the remaining black residue was filtered, washed with water and dried. A black powdery material remained which was refluxed with 1 liter of xylene, filtered and the process repeated with the solid residue. On cooling, a slightly brown-colored material crystallized. The quinoline thus obtained was purified from xylene; brownish yellow crystals, m. p. 197–198° (cor.); yield 30 g. (45%).

*Anal.* Calcd. for  $C_{21}H_{14}N_2O_3S$ : C, 67.35; H, 3.77; N, 7.49. Found: C, 67.59; H, 3.73; N, 7.45.

**5-Aminobenzofuro[3,2-f]quinoline (XIII).**—To 7 g. of the sulfonamide, 17 cc. of sulfuric acid (prepared from 3 volumes of concentrated sulfuric acid and 1 volume of water) was added and the mixture was heated for twenty minutes in an oil-bath at 145° (bath temperature). Water was added after cooling and the red solution made alkaline and refluxed. After cooling, the amine was filtered, dried and purified by recrystallization from petroleum ether (b. p. 60–110°); yellow crystals, m. p. 139–140° (cor.); yield, 3.3 g. (78%).

*Anal.* Calcd. for  $C_{18}H_{10}N_2O$ : C, 76.91; H, 4.30; N, 11.96. Found: C, 77.18; H, 4.45; N, 11.44.

Concentrated hydrochloric acid with or without glacial acetic acid, sodium in liquid ammonia or sodium amide were all unsatisfactory reagents for hydrolysis.

**5-[4-Diethylamino-1-methylbutylamino]benzofuro[3,2-f]quinoline (XIV).**—A mixture of 4.7 g. of 5-aminobenzofuro[3,2-f]quinoline and 4.2 g. of 4-chloro-N,N-diethylamylamine hydrochloride was heated in an atmosphere of nitrogen to 180°. When the temperature reached about 100° the mixture liquefied and was thoroughly shaken. On raising the temperature a red paste was obtained which was heated for two hours at 180°. After cooling the material was transferred into a three-necked flask with 30 cc. of *n*-butanol. Another 10 g. of 4-chloro-N,N-diethylamylamine hydrochloride was added and 3 g. of anhydrous potassium carbonate and the mixture heated with mechanical stirring for thirty hours at 140–150°. At this point 2 cc. of 1-diethylamino-4-pentanol was added. Heating and stirring were continued for another thirty hours. The solvent was evaporated and the residue shaken with 10% aqueous sodium hydroxide and extracted with

benzene. The benzene layer was washed with water several times. The residue obtained by evaporation of the benzene was boiled with 500 cc. of petroleum ether (b. p. 60–110°) and filtered. On cooling, the unreacted aminoquinoline was obtained as yellow crystals. More of this starting amine was obtained on concentrating the petroleum ether solution. The product was distilled at 0.01 mm. The excess 1-diethylamino-4-pentanol was much lower boiling than the desired alkylated amine which was distilled at a bath temperature of 230–250°. The distillate was dissolved in 80 cc. of petroleum ether and more of the unalkylated amine separated after cooling at 4° for twenty-four hours. The petroleum ether again was evaporated and the resulting viscous material distilled at 0.01 mm. The first few drops of the distillate were discarded because they contained most of the starting amine still present. Finally 1.8 g. of product was obtained as a red viscous oil which still contained a small amount of unalkylated amine.

*Anal.* Calcd. for  $C_{24}H_{29}N_3O$ : C, 76.67; H, 7.78. Found: C, 77.14; H, 7.63.

The presence of potassium iodide did not improve the yield of alkylated amine.

**Deamination of 5-Aminobenzofuro[3,2-f]quinoline (XIII).**—The amine (0.2 g.) was dissolved in 35 cc. of hot concentrated hydrochloric acid and the resulting solution cooled to 0°. The suspension thus obtained was diazotized rapidly with 0.088 g. of sodium nitrite in 5 cc. of water. After five minutes at 0–3°, the diazonium solution was filtered quickly and to the clear filtrate 35 cc. of ice-cold 50% aqueous hypophosphorous acid was added. The reaction mixture was allowed to stand in the refrigerator for twelve hours, followed by an additional twelve hours at room temperature. The solution was made alkaline with aqueous sodium hydroxide and the precipitate which formed was filtered, washed with a little water and dried. After two "short path" distillations at a pressure of 2 mm. and a bath temperature of 100–120°, 0.090 g. of needles which melted at 81–82° was obtained. The product was recrystallized from petroleum ether (b. p. 35–60°); very pale yellow needles, m. p. 82–83.5° (cor.). The melt

solidified and remelted at the same value. The product is insoluble in Claisen potash solution and gives a negative ferric chloride test and a negative Beilstein test for halogens.

*Anal.* Calcd. for  $C_{15}H_9NO$ : C, 82.17; H, 4.14; N, 6.39. Found: C, 82.13; H, 4.42; N, 6.41.

### Summary

1. Benzofuro[3,2-g]quinoline was nitrated to a single mononitro derivative. By reduction the corresponding amino compound was synthesized and converted into 3-diethylaminopropylamino and 3-(4-morpholinyl)-propylamino derivatives. Neither showed antimalarial activity.

2. Benzofuro[2,3-f]quinoline yielded two difficultly separated mononitro derivatives. The corresponding amines and, through them, the corresponding bromo compounds were synthesized.

3. 5-Nitrobenzofuro[2,3-f]quinoline was synthesized from 2-nitro-3-aminodibenzofuran. It was then reduced, and the morpholinylpropyl derivative prepared. This latter compound had no antimalarial activity.

4. 3-Benzenesulfonamido-2-nitrodibenzofuran was reduced to the corresponding amine which, in turn, was converted by means of a Skraup synthesis to the benzenesulfonamidobenzofuroquinoline. This last compound was hydrolyzed to the aminobenzofuroquinoline and attempts made to substitute the amino group with appropriate alkyl radicals.

URBANA, ILLINOIS

RECEIVED JULY 31, 1943

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

## Studies on Lignin and Related Compounds. LXXIV. Relation of Wood Ethanolysis Products to the Hibbert Series of Plant Respiratory Catalysts. Allylic and Dismutation Rearrangements of 3-Chloro-1-(3,4-dimethoxyphenyl)-2-propanone and 1-Bromo-1-(3,4-dimethoxyphenyl)-2-propanone

BY ARTHUR M. EASTHAM,<sup>1</sup> H. E. FISHER,<sup>1</sup> MARSHALL KULKA AND HAROLD HIBBERT

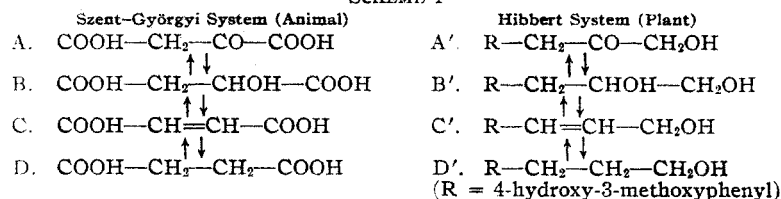
In previous communications<sup>2,3</sup> on the origin and function of lignin in the plant, a comparison

catalysts<sup>4</sup> and a suggested analogous system composed of assumed lignin progenitors capable of functioning in a similar manner in the plant cell (Scheme 1).

The third member of the Hibbert system, coniferyl alcohol (C') (corresponding to fumaric acid in the animal system), is known to be present in practically all plants in the early stages of growth.<sup>5</sup> The non-appearance of this and the other three members among

the lignin fission products isolated in the ethanolysis of wood is assumed to be due to their very labile character, resulting in their ready conver-

SCHEME 1



was drawn between the Szent-Györgyi animal cell system of hydrogen-transporting respiratory

(1) Holder of a National Research Council of Canada Studentship 1941–1942.

(2) Hibbert, *Paper Trade J.*, **113**, No. 4, 35 (1941).

(3) Hibbert, *Ann. Rev. Biochem.*, **11**, 183 (1942).

(4) Szent-Györgyi, *Ber.*, **72A**, 53 (1939).

(5) Czapek, "Biochemie der Pflanzen," Vol. III, G. Fischer, Jena, 1921, p. 464.