as described by E. Fischer[19] except that it was found unnecessary to heat the hydrochloric acid to effect solution of the sugar (finely powdered). The mercaptal (8 g.) was acetylated overnight with pyridine (32 cc.) and acetic anhydride (64 cc.) and crystallization of the product took place immediately on pouring into 1 liter of ice and water. Pure material was obtained on recrystallization from methanol by the addition of water; yield 13.9 g., m. p. 99–100°, spec. rot. −12° (25°; *c*, 4; U. S. P. $CHCl_3$). The substance crystallized in fine prisms and was soluble in the common solvents except water and petroleum ether.

Anal. Calcd. for $C_9H_{18}O_6S_2(CH_3CO)_6$: S, 11.3; CH_3CO, 10.6 cc. 0.1 *N* NaOH per 100 mg. Found: S, 11.2; CH_3CO, 10.6 cc.

Demercaptalation of *d*-α-glucoheptose hexaacetate yielded sirups which were not amenable to crystallization.

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Summary

1. The methyl hemiacetal and the aldehydrol (with one mole of acetone of crystallization) of *aldehydo-d*-mannose pentaacetate have been synthesized.

2. 1-Bromo-*aldehydo-d*-mannose hexaacetate and 1-bromo-*aldehydo-l*-rhamnose pentaacetate have been synthesized.

3. Two stereoisomeric forms (denoted as α and β) of the 1-methoxy-1-acetate of the *aldehydo*-acetates of *d*-glucose, *d*-mannose, *d*-galactose and *l*-arabinose have been synthesized. The synthesis of the second isomer of the corresponding 1-ethoxy derivative of *d*-galactose is reported.

4. 1-Bromo-*aldehydo-d*-galactose hexaacetate and 1-chloro-1-ethoxy-*aldehydo-d*-galactose pentaacetate have been converted to *aldehydo-d*-galactose pentaacetate ethyl hemiacetal.

5. 1-Chloro-1-methoxy-*aldehydo-d*-mannose pentaacetate has been synthesized.

6. The dimethyl and diethyl acetals (and their tetraacetates) of *l*-arabinose have been synthesized from *l*-arabinose diethyl mercaptal.

7. *d*-Gluco-*d*-gulo-heptose diethyl mercaptal hexaacetate has been synthesized.

8. All compounds reported have been obtained in pure, crystalline condition.

COLUMBUS, OHIO RECEIVED JULY 8, 1940

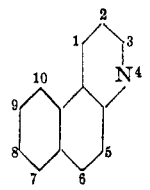
(19) E. Fischer, *Ber.*, **27**, 673 (1894).

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Nitro and Aminobenzo[f]quinolines and Derivatives

BY W. JACK CLEM[1] AND CLIFF S. HAMILTON

At the beginning of this investigation, which had for its purpose the study of benzo[f]quinolines with substituents in the benzo-ring, the only mononitro derivative recorded was 7-nitrobenzo[f]quinoline, first prepared by Claus and Besseler[2] by the direct nitration of benzo[f]quinoline.



Benzo[f]quinoline

They also reported the corresponding amine and later Armit and Robinson[3] established its structure and thereby that of the nitro compound.

Small amounts (10 g.) of benzo[f]quinoline, prepared by a modification of the method of Knueppel,[4] were nitrated successfully at temperatures of −15° to −10° to give 7-nitrobenzo[f]-quinoline, but attempts to carry out the reaction with 50-g. quantities gave mixtures containing large quantities of a dinitrobenzo[f]quinoline from which it was almost impossible to separate pure 7-nitrobenzo[f]quinoline. The dinitrobenzo[f]quinoline was shown to be identical with that obtained by Hepner[5] by reducing to the corresponding diamine and the structure was demonstrated by nitrating 7-nitrobenzo[f]quinoline to give the same compound. This established one nitro group in the 7-position and as Hepner[5] had already shown that the groups are in meta positions with respect to each other and both are in the benzo-ring, the compound must be 7,9-dinitrobenzo[f]quinoline, and the corresponding diamine is 7,9-diaminobenzo[f]quinoline.

(1) Parke, Davis and Company Fellow.

(2) Claus and Besseler, *J. prakt. Chem.*, [2] **57**, 49 (1898).

(3) Armit and Robinson, *J. Chem. Soc.*, **127**, 1604 (1925).

(4) Knueppel, *Ber.*, **29**, 703 (1896).

(5) Hepner, *Sitzber. Akad. Wiss. Wien, Math.-naturw. Klasse. Abt. IIb*, **115**, 847 (1906).

Considerable difficulty was encountered in the preparation of both 8-nitro- and 10-nitrobenzo[f]quinoline. The most successful method found was based on the use of both ferrous sulfate[6] and boric acid[7] in the reaction. Anhydrous glycerol gave better yields than technical glycerol although water was introduced into the reaction by the use of sirupy (85%) arsenic acid.

8-Nitrobenzo[f]quinoline proved to be almost insoluble in all common organic solvents with the exception of glacial acetic acid. Because of this, purification was difficult. Continuous crystallization from ether using a Soxhlet extractor was most successful although it was very slow.

The three isomeric aminobenzo[f]quinolines were prepared by catalytic reduction with molecular hydrogen. 7-Aminobenzo[f]quinoline, reported by Claus and Besseler,[2] appeared to be more stable than these authors had thought. 8-Aminobenzo[f]quinoline did not darken in contact with the atmosphere but 10-aminobenzo[f]-quinoline oxidized so rapidly that it was necessary to isolate it in an atmosphere of carbon dioxide. 8-Aminobenzo[f]quinoline forms a dihydrochloride but does not appear to form a monohydrochloride. Both 7-amino- and 10-aminobenzo[f]quinoline form monohydrochlorides which can be converted to dihydrochlorides under suitable conditions. These dihydrochlorides are less stable than the monohydrochlorides.

Numerous attempts were made to alkylate 7-aminobenzo[f]quinoline without success. Neither did propylene oxide react with this amine during six hours at 100° under pressure. However, the amine was acetylated with acetic anhydride in glacial acetic acid solution. It also condensed with benzaldehyde and *m*-nitrobenzaldehyde. 10-Aminobenzo[f]quinoline acetylated easily but an attempt to condense it with benzaldehyde yielded only an oil. 8-Benzalaminobenzo[f]-quinoline was obtained only with difficulty and then the reaction gave a lower yield than is common for the reaction between primary amines and benzaldehyde.

8-Aminobenzo[f]quinoline and 10-aminobenzo[f]quinoline were oxidized to quinoline-5,6-dicarboxylic acid[5] in order to prove that the Skraup reaction caused ring closure to take place on the α-carbons of the nitro-2-naphthylamines rather than on the second β-carbon atoms.

(6) Clarke and Davis, "Organic Syntheses," Vol. II, 1922, p. 79.
(7) Cohn, THIS JOURNAL, **52**, 3685 (1930).

Treatment of 1-methyl-3-chlorobenzo[f]quinoline with ethanolamine gave a good yield of 1-methyl-3-β-hydroxyethylaminobenzo[f]quinoline. The action of phosphorus oxychloride on this compound resulted not in the replacement of the hydroxyl group by chlorine but in dehydration to give an unsaturated side chain containing no halogen. If there were no rearrangement of hydrogen and double bonds (prototropy) this reaction would lead to 1-methyl-3-vinylaminobenzo[f]quinoline. However, the product had a bright orange-yellow color suggesting that rearrangement may have taken place to form 1-methyl-3-ethylidineaminobenzo[f]quinoline.

Experimental

Benzo[f]quinoline.—A suspension of 100 g. of arsenic acid and 100 g. of 2-naphthylamine in 215 g. of glycerol was heated to 140° while well stirred. About one-half of 200 g. of concd. sulfuric acid was added in large portions and the remainder dropwise after the solid which first formed had dissolved. The mixture was refluxed at 150–155° for four hours, poured into 2 liters of water, allowed to stand overnight and filtered. The filtrate was neutralized by dropwise addition of 6 *N* sodium hydroxide with extremely rapid mechanical agitation. The crystalline mass was filtered, dried and dissolved in acetone. The hydrochloride was precipitated by saturating the solution with dry hydrogen chloride, filtered, dissolved in water, charcoaled and the free base again precipitated by neutralizing with 6 *N* sodium hydroxide; yield 102 g. or 81.5% (Knueppel[4] reported 74%); recrystallized from alcohol-water mixture, m. p. 93°.

7-Nitrobenzo[f]quinoline.—A solution of 10 g. of benzo[f]quinoline in 30 ml. of concd. sulfuric acid was cooled to −15° and nitrated by the slow addition of a mixture of 2.55 ml. of fuming nitric acid (d. 1.50) and 10 ml. of concd. sulfuric acid which had previously been cooled to the same temperature. Stirring was continued for fifteen minutes, after which the mixture was poured into 1.5 kg. of ice and water, neutralized with 6 *N* sodium hydroxide and filtered. The crystalline mass was twice recrystallized from 95% alcohol with charcoaling; yield 5 g. or 40%; m. p. 174°. Hepner[5] reported m. p. 173°.

8-Nitrobenzo[f]quinoline.—To a mixture of 2 g. of ferrous sulfate and 9.4 g. of 6-nitro-2-naphthylamine was added 18 ml. of anhydrous glycerol, in which 6 g. of boric acid had previously been dissolved. Next 5 ml. of sirupy (85%) arsenic acid and finally 10 ml. of concentrated sulfuric acid were added, the latter slowly and with cooling. The mixture was heated at 140° under reflux for ten hours and poured into 600 ml. of water. The aqueous solution was allowed to stand overnight, heated to 80°, filtered, and the hot solution made alkaline with 6 *N* sodium hydroxide. The precipitate was filtered and dried at 100°. The crude product was first recrystallized from glacial acetic acid and finally purified by recrystallizing from ether; yield 3.8 g.

10-Nitrobenzo[f]quinoline.—This compound was synthesized from 8-nitro-2-naphthylamine in a manner identi-

cal with that for 8-nitrobenzo[f]quinoline. The crude product was twice recrystallized from 95% alcohol with charcoaling; yield 3.75 g.

7,9-Dinitrobenzo[f]quinoline.—A solution of 50 g. of benzo[f]quinoline in 200 ml. of concd. sulfuric acid was cooled to 0°. To this was added dropwise a mixture of 37.5 g. of fuming nitric acid (d. 1.50) and 75 g. of concd. sulfuric acid. The mixture was poured into 1.5 kg. of ice and water and neutralized with 6 *N* sodium hydroxide. The precipitate was filtered and dried. Repeated fractional crystallizations from acetone gave a least soluble fraction which analyzed for a dinitrobenzo[f]quinoline; m. p. 250°. Hepner[5] gave 249° as the melting point of a dinitrobenzo[f]quinoline made by nitrating benzo[f]quinoline at 100°.

7,9-Dinitrobenzo[f]quinoline was also prepared by nitrating 7-nitrobenzo[f]quinoline: to a solution of 0.5 g. of 7-nitrobenzo[f]quinoline in 3 ml. of concd. sulfuric acid was added a mixture of 0.3 ml. of fuming nitric acid (d. 1.50) and 0.7 ml. of concd. sulfuric acid. The mixture was heated on a water-bath for two hours, poured on ice and neutralized with 6 *N* sodium hydroxide. The precipitate was filtered, twice recrystallized from ethyl alcohol with charcoaling and finally recrystallized from acetone. No depression of melting point was exhibited when mixed with the compound prepared from benzo[f]quinoline.

7-Aminobenzo[f]quinoline.—A solution of 5.4 g. of 7-nitrobenzo[f]quinoline in acetone was reduced at room temperature with electrolytic hydrogen under 40 pounds (2.67 atm.) pressure using, as a catalyst, Raney nickel prepared by the method of Adkins.[8] The catalyst was removed by filtering and the filtrate was concentrated and diluted with water until just saturated while hot and then allowed to cool. The crude precipitate was filtered and recrystallized from an alcohol–water (or acetone–water) mixture to which a few drops of ammonium hydroxide had been added. The compound was dried and stored in a vacuum desiccator over sodium hydroxide; yield 4.6 g.; m. p. 175°. Claus and Besseler[2] reported the compound as melting at 158°.

8-Aminobenzo[f]quinoline.—A suspension of 3 g. of 8-nitrobenzo[f]quinoline was reduced as described above. The crude precipitate was recrystallized from ethyl alcohol.

10-Aminobenzo[f]quinoline.—A suspension of 3 g. of 10-nitrobenzo[f]quinoline in acetone was reduced as described above. The acetone solution was concentrated, diluted with water and allowed to cool under an atmosphere of carbon dioxide. The resulting precipitate was charcoaled and recrystallized from ethyl alcohol, still under an atmosphere of carbon dioxide. The product was dried in a vacuum desiccator over sodium hydroxide to give white needles which darkened rapidly when exposed to air.

7,9-Diaminobenzo[f]quinoline.—A suspension of 1.75 g. of 7,9-dinitrobenzo[f]quinoline in acetone was reduced as described in the case of 7-aminobenzo[f]quinoline. A strongly fluorescent solution remained after the catalyst was filtered. This was saturated with dry hydrogen chloride to give a red hydrochloride which was filtered and dissolved in water. The free base was precipitated by the dropwise addition of 6 *N* sodium hydroxide solution and was then recrystallized from ethyl alcohol to give dark brown microscopic crystals melting at 245–246°. The diamine prepared by Hepner[5] had similar colors both as the free base and as the hydrochloride and melted at 249°.

7-Acetaminobenzo[f]quinoline.—To a solution of 1.00 g. of 7-aminobenzo[f]quinoline in 4 ml. of glacial acetic acid was added 0.6 ml. of acetic anhydride. No heat was evolved, but on standing a semi-solid mass formed which was dissolved by addition of water and then neutralized with ammonium hydroxide to give a yellow, crystalline product. This was filtered and recrystallized from an alcohol–water mixture to give white needles.

10-Acetaminobenzo[f]quinoline was prepared in the same manner.

7-Benzalaminobenzo[f]quinoline.—To a solution of 1.55 g. of 7-aminobenzo[f]quinoline in boiling alcohol was added 0.81 ml. of benzaldehyde. The solution was boiled for five minutes, after which water was added until the hot solution was saturated. It was allowed to cool and crystallize, was filtered and recrystallized, first from an alcohol–water mixture and finally from 95% ethyl alcohol. The product was dried in a vacuum desiccator over sodium hydroxide.

7-Benzylaminobenzo[f]quinoline.—A solution of 2.15 g. of 7-benzalaminobenzo[f]quinoline in acetone was reduced with molecular hydrogen as described previously. The precipitated solid was recrystallized from methyl alcohol and dried in a vacuum desiccator over sodium hydroxide.

7-*m*-Nitrobenzalaminobenzo[f]quinoline was prepared in the same manner as the 7-benzalamino derivative. The product was recrystallized from methyl alcohol.

7-*m*-Aminobenzylaminobenzo[f]quinoline was prepared by the procedure for the 7-benzylamino derivative. The yellow product was recrystallized from an alcohol–water mixture and dried in a vacuum desiccator over sodium hydroxide. It decomposed slowly upon standing even under vacuum.

8-Acetaminobenzo[f]quinoline.—To a solution of 0.5 g. of 8-aminobenzo[f]quinoline in glacial acetic acid was added 1 ml. of acetic anhydride. The solution was heated to boiling for five minutes, cooled, diluted to three times its volume with water and made basic with ammonium hydroxide solution, at which time a white precipitate appeared. The suspension was again boiled for five minutes, cooled, and filtered. The product was recrystallized from alcohol and dried at 65°.

8-Benzalaminobenzo[f]quinoline.—A solution of 1.2 g. of 8-aminobenzo[f]quinoline and 0.75 ml. of benzaldehyde in absolute ethyl alcohol was refluxed for three hours. The hot solution was saturated by addition of water, allowed to cool, and the product was recrystallized from ethyl alcohol.

1-Methyl-3-β-hydroxyethylaminobenzo[f]quinoline.—A solution of 9.5 g. of 1-methyl-3-chlorobenzo[f]quinoline in 45 ml. of ethanolamine was refluxed at 180° for nine hours. At the end of this time the reaction mixture was poured into water, forming a gum which soon crystallized. The product was filtered and recrystallized from ethyl alcohol solution after charcoaling.

1-Methyl-3-vinylaminobenzo[f]quinoline.—A mixture of 10 g. of 1-methyl-3-β-hydroxyethylaminobenzo[f]quinoline and 50 ml. of phosphorus oxychloride was heated under reflux for two hours at 110°. The reaction mixture was al-

(8) Covert and Adkins, THIS JOURNAL, **54**, 4116 (1932).

TABLE I

Compound	Yield, %	Description	M. p., °C.		Analyses, % Found	Calcd.
8-Nitrobenzo[f]quinoline	34	Yellow needles	240	N	12.43	12.50
10-Nitrobenzo[f]quinoline	34	White needles	145	N	12.42	12.50
7,9-Dinitrobenzo[f]quinoline		White needles	250	C	58.10	57.99
				H	2.75	2.62
7-Aminobenzo[f]quinoline	90	Yellow needles	175			
8-Aminobenzo[f]quinoline	90	White plates	222-224	C	80.22	80.38
				H	5.34	5.19
10-Aminobenzo[f]quinoline	85	White needles	156–157	C	80.25	80.38
				H	5.27	5.19
7,9-Diaminobenzo[f]quinoline		Brown crystals	245–246			
7-Aminobenzo[f]quinoline monohydrochloride	90	Brick-red micro. needles	>300	Cl	15.61	15.42
7-Aminobenzo[f]quinoline dihydrochloride	90	Tan micro. needles	>300	Cl	26.45	26.54
8-Aminobenzo[f]quinoline dihydrochloride	90	Brown micro. needles	>300	Cl	26.37	26.54
10-Aminobenzo[f]quinoline monohydrochloride	90	Orange micro. needles	>300	Cl	15.23	15.42
10-Aminobenzo[f]quinoline dihydrochloride	90	White needles	>300	Cl	26.10	26.54
Quinoline-5,6-dicarboxylic acid		White prisms	230–240			
7-Acetaminobenzo[f]quinoline	85	White needles	235	C	76.07	76.25
				H	5.10	5.12
7-Benzalaminobenzo[f]quinoline	90	Yellow micro. cryst.	101	N	9.85	9.92
7-Benzylaminobenzo[f]quinoline	90	Yellow plates	152–154	C	84.30	84.47
				H	5.80	5.67
7-*m*-Nitrobenzalaminobenzo[f]quinoline	83	Orange-yellow cryst.	182–183	C	73.44	73.38
				H	4.16	4.00
7-*m*-Aminobenzylaminobenzo[f]quinoline	90	Unstable yellow pwd.	141–144	N	13.95	14.04
8-Acetaminobenzo[f]quinoline	83	Glistening white plates	212–213	N	11.03	11.86
8-Benzalaminobenzo[f]quinoline	46	Yellow-orange pwd.	148–151	N	9.78	9.92
10-Acetaminobenzo[f]quinoline	73	White plates	152–154	N	12.02	11.86
1-Methyl-3-β-hydroxyethylaminobenzo[f]quinoline	77	White plates	148–149	N	11.07	11.11
1-Methyl-3-vinylaminobenzo[f]quinoline		Orange-yellow needles	163–164	C	81.96	82.02
				H	6.18	6.02
				N	11.82	11.96

lowed to cool and poured slowly into ice water. After the aqueous solution had cooled, it was made distinctly basic to litmus with ammonium hydroxide and evaporated to a small volume. The solid which formed on cooling was filtered, dissolved in ethyl alcohol, boiled and filtered and the filtrate was evaporated to a small volume, cooled and again filtered. The resulting yellow solid was dissolved in water, the solution was made basic with 1 *N* sodium hydroxide solution and the orange-yellow precipitate filtered. The product was recrystallized from isopropyl alcohol to which a few drops of ammonium hydroxide had been added. The compound contained no halogen and decolorized cold permanganate solution.

Summary

8-Nitrobenzo[f]quinoline and 10-nitrobenzo[f]quinoline were prepared for the first time from 6-nitro- and 8-nitro-2-naphthylamine, respectively, by means of the Skraup reaction.

The three isomeric nitrobenzo[f]quinolines were reduced to the corresponding amines and these were compared by preparing the aminobenzo[f]quinoline hydrochlorides, acetylaminobenzo[f]quinolines and benzalaminobenzo[f]quinolines.

It was shown that benzo[f]quinoline nitrates even at 0° to give a dinitro derivative. This was identical with the dinitro derivative prepared by Hepner by nitrating at 100°. This compound was shown to have the structure of 7,9-dinitrobenzo[f]quinoline and the corresponding diamine is 7,9-diaminobenzo[f]quinoline.

1-Methyl-3-β-hydroxyethylaminobenzo[f]quinoline and 1-methyl-3-vinylaminobenzo[f]quinoline were prepared from 1-methyl-3-chlorobenzo[f]quinoline.

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