intensities of radiation transmitted by the solvent and by the solution when the spectrometer is set at frequency ν, the adsorption maximum, and B is the bandwidth in wave numbers at log $\frac{\left(\frac{T_0}{T}\right)_\nu}{2}$. Small satellite bands associated with the carbonyl band were ignored in the calculation. We thank Philip Launer for making the measurements and calculations.

DISCUSSION

The areas under the carbonyl band for four anthraquinones are:

Methyl 1-anthraquinonesulfenate	8,200
1-Anthraquinonesulfenyl bromide	7,000
1-Anthraquinonylmethyl sulfide	13,000
1-Mercaptoanthraquinone	13,000

The two compounds for which a tetracyclic structure is proposed have only about half the band area of the two that unequivocally have two carbonyl groups. The smaller area shows that one carbonyl group has disappeared. Measurements of the carbonyl band area made with the acid itself were not reproducible and were considered unreliable for the concentration of the acid was in doubt. After standing a few minutes, chloroform solutions of the acid became filled instantaneously with copious precipitate. Apparently the sulfenic acid had reacted with itself and formed a supersaturated solution. The precipitate, which melted above 300°, was probably the anhydride, which is known to form on heating a solution of the acid.[1] A tetracyclic structure for the acid is proposed by analogy.

An interesting difference between the reactions of 1-anthraquinonesulfenic acid and its salts is explained by the tetracyclic structure for the free acid. Reaction of the free acid with methyl alcohol or methyl sulfate yielded "methyl 1-anthraquinonesulfenate",[9] but reaction of the sodium or potassium salt with methyl sulfate gave exclusively methyl 1-anthraquinonyl sulfoxide. These differences in behavior had been attributed to an unlikely "pseudo" structure R–S(H)–O for the acid.[10] The present explanation based on a gross difference in structure between the free acid and its salt accounts for the formation of different products with the same reagent more satisfactorily.

1-Anthraquinonesulfenic acid dissolves in aqueous or alcoholic solutions of sodium or potassium hydroxide, sodium carbonate, or ammonia to form solutions of characteristic color.[1] The tetracyclic structure for the acid is not incompatible with this behavior; nucleophilic attack on the sulfur would be expected to open the ring readily with formation of the sulfenic acid salt.

(9) Fries and Schurmann, *Ber.*, **52**, 2182 (1919).
(10) Gutmann, *Ber.*, **41**, 1650 (1908).

Failure to isolate 1-fluorenonesulfenic acid[3] does not militate against the new structure for 1-anthraquinonesulfenic acid. Divergence of the benzene rings at the carbonyl end of the fluorenone molecule results in a prohibitive bonding distance between the carbonyl oxygen and the sulfur atom. Models can be made of the structure now proposed for 1-anthraquinonesulfenic acid but not of the analogous structure for fluorenone.

A further possible method of proof of structure would be optical resolution of the sulfenic acid or a derivative. The proposed structure contains an asymmetric center; the others do not. The esters at least are probably stable enough to survive the necessary handling. The methyl ester has been refluxed in ethanol for six hours in our laboratory without change.

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The Diazotization of 3-Aminoisoquinoline[1]

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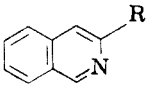
The transformation of 3-aminoisoquinoline (I) into 3-bromo- and 3-fluoro-isoquinoline was recently reported.[3,4] Diazotization of this amine and replacement of the diazo group by hydroxyl (II) and acetoxy (III) groups has now been realized.[5]



R = NH_2 (I); OH (II); $OCOCH_3$ (III); $NHCONH_2$ (IV).

In agreement with the earlier work, 3-chloroisoquinoline together with unidentified material resulted from the diazotization of the corresponding amine in dilute hydrochloric acid. Diazotization in dilute sulfuric acid, however, allowed the formation of 3-hydroxyisoquinoline in low yield together with an unidentified product in which the heterocyclic ring was apparently destroyed. This same compound was subsequently obtained upon the treatment of 3-hydroxyisoquinoline with nitrous acid.

From the combination of 3-aminoisoquinoline and isoamyl nitrite in glacial acetic acid at room

(1) A National Science Foundation Grant in support of this work is gratefully acknowledged.
(2) Texas Eastman Fellow 1955–1956.
(3) F. H. Case, *J. Org. Chem.*, **17**, 471 (1952).
(4) A. Roe and C. E. Teague, Jr., *J. Am. Chem. Soc.*, **73**, 687 (1951).
(5) An unidentified product from the decomposition of 3-isoquinoline diazonium fluoroborate was thought to be 3-hydroxyisoquinoline. It gave a strong positive ferric chloride test.[4]

temperature, a good yield of 3-acetoxyisoquinoline was obtained. This has provided one of the rare examples of the transformation of an aryl diazonium acetate, or the tautomeric N-nitrosoacetamide, into the corresponding phenol acetate and nitrogen.[6] An unexpected yellow color of 3-amino and 3-hydroxyisoquinoline was not shared by the colorless 3-acetoxyisoquinoline, 3-isoquinolylurea and the sodium salt of 3-hydroxyisoquinoline. Apparently tautomerization is required to explain the presence of the yellow chromophore. The ester showed marked resistance to attack by water but was saponified upon shaking with dilute sodium hydroxide for several hours. The two known isomers, 5- and 7-acetoxyisoquinoline were, in contrast, unstable to storage and were rapidly saponified.[7] Hydrolysis of 2-acetoxypyridine occurred readily in water,[8] and the esters of 2-quinolinol were more readily hydrolyzed than those of 3-, 5-, 6-, 7-, and 8-quinolinol.[9]

EXPERIMENTAL[10]

Diazotization of 3-aminoisoquinoline in 5% aqueous sulfuric acid. A solution of 0.22 g. (1.5 mmoles) of 3-aminoisoquinoline,[3,4] 5 ml. of water, and 0.59 g. (5.9 mmoles) of concentrated sulfuric acid was externally cooled by an ice and salt bath and stirred mechanically. A temperature of 0–5° was maintained during the dropwise addition of a solution containing 0.31 g. (4.5 mmoles) of sodium nitrite. A yellow precipitate of crude 3-hydroxyisoquinoline sulfate [0.08 g. (26.6%), m.p. 221–226° (dec.)], was collected after stirring for an additional five to ten minutes. Upon recrystallization from alcohol, 3-hydroxyisoquinoline sulfate separated as a yellow powder, m.p. 235–236°. An alcoholic solution of this compound gave a red color with ferric chloride and a positive test for sulfate ion was obtained with barium chloride solution.

Anal. Calc'd for $C_{18}H_{14}N_2O_2 \cdot H_2SO_4$: C, 55.66; H, 4.16; N, 7.22. Calc'd for $C_{18}H_{14}N_2O_2 \cdot H_2SO_4 \cdot {}^1/_2H_2O$: C, 54.51; H, 4.31; N, 7.05. Found: C, 54.84; H, 4.57; N, 6.98.

After shaking 0.1 g. (0.7 mmole) of crude 3-hydroxyisoquinoline sulfate with 1.5 ml. of 2 *N* sodium hydroxide for two hours a white precipitate of the sodium salt of 3-hydroxyisoquinoline was collected by filtration. Upon treatment with aqueous acetic acid a total of 0.05 g. (18% conversion from 3-aminoisoquinoline) of 3-hydroxyisoquinoline was obtained and recrystallized from ethanol from which it separated as yellow needles, m.p. 195–196°. It was identical with the product obtained upon saponification of 3-acetoxyisoquinoline (see below).

This sample of 3-hydroxyisoquinoline was dissolved in 2 ml. of 1 *N* sodium hydroxide and then was treated with acetic anhydride. Upon cooling, white crystals of 3-acetoxyisoquinoline were collected, m.p. 83–85° (see below).

The filtrate from the diazotization reaction from which the 3-hydroxyisoquinoline sulfate was separated was allowed to stand overnight. A light yellow crystalline precipitate, 0.14 g., was dissolved in ethanol, acidified with a few drops of hydrochloric acid, boiled with Nuchar (charcoal), filtered, and the filtrate was concentrated under a stream of nitrogen. A yellow precipitate was separated and the filtrate was diluted with water and chilled. A precipitate of colorless needles, m.p. 210–211° (dec.), was recrystallized from ethanol with no change in melting point and dried in a vacuum desiccator over phosphorus pentoxide.

Anal. Calc'd for $(C_{15}H_{13}N_3O_5)_n$: C, 57.16; H, 4.17; N, 13.33; O, 25.38. Found: C, 56.99; H, 4.42; N, 13.33; O, 25.03.

Strong absorption in the infrared occurred at 3.14–3.18 (possibly an associated hydroxyl group), 3.32, 3.51, 6.00 (possibly an amide carbonyl), 6.18, 6.63, 6.74, 6.84, 7.04, 7.48, 8.02, 9.16–9.23, 9.77, 10.08–10.11, 12.36–12.43, 12.80, and 12.98–13.08 microns.

Reaction of 3-hydroxyisoquinoline with sulfuric acid. A solution of 0.05 g. (0.34 mmole) of 3-hydroxyisoquinoline, 5 ml. of water, and 0.1 g. (1.0 mmole) of concentrated sulfuric acid was stirred for 30 minutes. Yellow 3-hydroxyisoquinoline sulfate, 0.02 g. (30.0%), m.p. 240–242°, was collected. No precipitate was observed when the filtrate was allowed to stand overnight. The filtrate was made basic with sodium bicarbonate and extracted with ether. Evaporation of the ether extract allowed recovery of unreacted 3-hydroxyisoquinoline.

Reaction of 3-hydroxyisoquinoline with nitrous acid. A solution of 0.07 g. (0.5 mmole) of 3-hydroxyisoquinoline in 1.6 ml. of water and 1.0 g. (10 mmoles) of concentrated sulfuric acid was cooled to 0–5°. A solution containing 0.07 g. (1.0 mmole) of sodium nitrite was added dropwise. No evolution of gas was observed during the addition; however, the solution changed in color from yellow to orange. After 15 minutes an impure yellow solid, m.p. 208–209° (dec.), was collected by filtration and washed with water. An additional sample of this product was obtained from the filtrate upon standing overnight as colorless needles, m.p. 208–209° (dec.), identical with the product obtained from the aqueous diazotization of 3-aminoisoquinoline.

Preparation of 3-acetoxyisoquinoline. To a solution of 0.43 g. (3.0 mmoles) of 3-aminoisoquinoline in 10 ml. of glacial acetic acid, 0.6 g. (5.0 mmoles) of isoamyl nitrite was added dropwise. Upon completion of the addition the solution was stirred for 15 minutes, diluted with water, and neutralized with sodium carbonate. A yellow precipitate of impure 3-acetoxyisoquinoline was obtained and recrystallized from the ethanol from which it separated as lustrous white plates, 0.36 g. (63.5%), m.p. 85–86°.

Anal. Calc'd for $C_{11}H_9NO_2$: C, 70.57; H, 4.86; N, 7.48. Found: C, 70.77; H, 4.86; N, 7.66.

A poorer yield (39%) of product together with an unidentified yellow compound was obtained upon carrying out the reaction in aqueous acetic acid at 0–5°.

An alcoholic solution of 3-acetoxyisoquinoline gave a red color with ferric chloride. Presence of an ester carbonyl group was indicated by infrared absorption at 5.66 μ.

Preparation of 3-hydroxyisoquinoline. A mixture of 0.72 g. (5.0 mmoles) of 3-acetoxyisoquinoline and 25 ml. of 2 *N* sodium hydroxide was shaken for 4 hours. A white precipitate of the sodium salt of 3-hydroxyisoquinoline was collected and treated with aqueous acetic acid. Long yellow needles, m.p. 198–199° from the preheated bath, of 3-hydroxyisoquinoline, 0.48 g. (86%), were obtained and

(6) The action of warm acetic acid upon diazotized 1-(*m*-nitrobenzeneazo)-2-aminonaphthalene brought about the formation of the corresponding phenol acetate [R. Meldola and F. J. East, *J. Chem. Soc.*, **53**, 460 (1888)]. See also O. Wallach, *Ann.*, **235**, 233 (1886); W. R. Orndorff, *Am. Chem. J.*, **10**, 368 (1888); E. H. White, *J. Am. Chem. Soc.*, **77**, 6014 (1955); Heyns and Bebenburg, *Ann.*, **595**, 69 (1955).

(7) R. B. Woodward and W. E. Doering, *J. Am. Chem. Soc.*, **67**, 860 (1945).

(8) A. E. Tschitschibabin and P. G. Szokow, *Ber.*, **58**, 2650 (1925).

(9) C. J. Cavallito and T. H. Haskell, *J. Am. Chem. Soc.*, **66**, 1166 (1944).

(10) Semi-micro analyses by Microtech Laboratories, Skokie, Illinois, and by Alfred Bernhardt, Microanalytisches Laboratorium, Muheim, (Ruhr), Germany. Infrared absorption data, obtained from potassium bromide wafers, were kindly provided by Mr. R. T. O'Connor of the Southern Utilization Research Branch, New Orleans, La.

recrystallized from 95% ethanol. Upon melting, the compound resolidified and then was charred at about 205°.

Anal. Calc'd for C_9H_7NO: C, 74.44; H, 4.87; N, 9.65. Found: C, 74.45; H, 4.82; N, 9.26.

Absorption in the infrared at 2.93 μ as well as a positive ferric chloride test suggested the presence of a phenolic hydroxyl group.

Preparation of 3-isoquinolylurea. The method of Kurzer[11] was followed. A solution of 1.4 g. (9.7 mmoles) of 3-aminoisoquinoline, 6 ml. of glacial acetic acid, and 10 ml. of water was warmed to 35–45°. A solution of 1.6 g. (9.7 mmoles) of potassium isocyanate in 10 ml. of water was warmed to 35–45° and added dropwise to the amine solution until a cloudiness appeared. The remainder of the isocyanate solution then was added all at once. The mixture was allowed to stand at room temperature for 2 hours and then was chilled in the refrigerator overnight. A light yellow precipitate of 3-isoquinolyl urea was collected and recrystallized from aqueous ethanol from which it separated as a white powder 1.0 g. (56%), m.p. 207–210°.

Anal. Calc'd for $C_{10}H_9N_3O$: N, 22.45. Found: N, 22.47.

Attempted nitrosation of 3-isoquinolylurea. A solution of 0.5 g. (2.7 mmoles) of 3-isoquinolylurea, 3.2 g. of concentrated sulfuric acid, and 5 ml. of water was cooled to 0–5°. The dropwise addition of a solution of 2.8 g. (4.1 mmoles) of sodium nitrite in 6 ml. of water was accompanied with vigorous gas evolution. The mixture was stirred for an additional 1.5 hours. A yellow-orange precipitate, 0.24 g., was collected, recrystallized from aqueous ethanol from which it separated as a yellow powder, m.p. 162–164°, and dried in the vacuum oven at 50° for 24 hours. Elementary analyses suggested the empirical formula, $C_{20}H_{18}N_6O_5$ for this unidentified product. The compound gave a positive Liebermann's nitroso test.

Anal. Calc'd for $C_{20}H_{18}N_6O_5$: C, 56.85; H, 4.30; N, 19.90. Found: C, 57.40; H, 4.37; N, 20.09.

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(11) F. Kurzer, *Org. Syntheses*, **31**, 8 (1951).

An Improved Method of Preparation of Side-Chain Labeled Cholesterol

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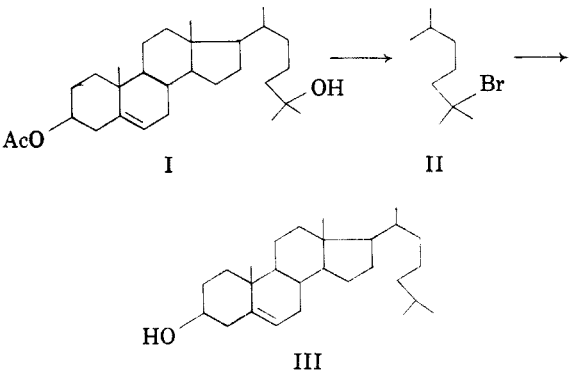
The conversion of 25-hydroxycholesteryl acetate[1,2] (I) to cholesterol (III) is of interest since the former compound is a readily prepared intermediate in the synthesis of cholesterol labeled with C^{14} at positions 24, 25, or 26. To date, two methods[1,2] have been reported for this conversion. In both instances, the 25-ol was first dehydrated to the 25-dehydro compound which, in turn, was either selectively hydrogenated directly or first converted to the 3,5-cyclo-6-ether and then hydrogenated. It has now been found that 25-bromocholesteryl acetate (II), an intermediate in the conversion of the 25-ol to the 25-dehydro compound, can be hydrogenated directly to cholesterol in alkaline solution in the presence of a moderately active Raney nickel catalyst. The over-all yield for this two-step conversion is 65%.



I II III

The intermediate 25-hydroxycholesteryl acetate was prepared by allowing methylmagnesium iodide to react with methyl 3β-hydroxy-Δ^5-homocholenate. In this manner, cholesterol-24-C^{14} was prepared by utilizing 3β-hydroxy-Δ^5-homocholenic acid-24-C^{14} which had been synthesized by chain elongation of the respective cholenic acid with C^{14}-diazomethane.[3]

EXPERIMENTAL[4]

Conversion of 25-hydroxycholesteryl acetate to cholesterol. The crystalline monoacetate[2] (490 mg.) was converted with phosphorus tribromide to 25-bromocholesteryl acetate as described previously,[2] and the bromide was recrystallized from acetone-water and dried in a high vacuum at room temperature; yield, 430 mg. (78%), m.p. 113–115° (lit.[2] m.p. 113.5–115.0°).

The recrystallized bromide (430 mg.) was dissolved in 80 ml. of 3.5% methanolic sodium hydroxide solution and was hydrogenated at a pressure slightly above atmospheric with a moderately active Raney nickel catalyst which had been prehydrogenated. Within 10–20 minutes, the theoretical amount of hydrogen was absorbed and then the catalyst was removed by filtration and washed with methanol. Potassium hydroxide (6.0 g.) was added to the filtrate and the solution was heated under reflux for 3 hours. The solution was concentrated under reduced pressure, the residue was cooled in ice, and a small volume of ether was added. The mixture was acidified with 1:1 hydrochloric acid, and the ethereal layer was separated, washed with water, and dried. After removal of the solvent, the residue was chromatographed on 12 g. of neutral alumina. With benzene-ether (1:1), 28 mg. (65%) of a crystalline material, m.p. 138–140°, was eluted. After recrystallization from methanol, the cholesterol melts from 145–146° and has an $[\alpha]_D^{25}$ −39.4° (*c*, 1.08, $CHCl_3$). The infrared spectrum was identical with that of an authentic sample.

Preparation of catalyst. The following method of Plattner and Pataki[5] was used. Raney nickel alloy (5 g.) was suspended in 20 parts of 4% aqueous sodium hydroxide solution and heated for 30 minutes on a steam-bath. This procedure was repeated with fresh sodium hydroxide solution

(1) A. I. Ryer, W. H. Gebert and N. M. Murrill, *J. Am. Chem. Soc.*, **72**, 4247 (1950).

(2) W. G. Dauben and H. L. Bradlow, *J. Am. Chem. Soc.*, **72**, 4248 (1950).

(3) The C^{14}-methylamine utilized in the preparation of labeled N-nitrosomethylurea was kindly supplied by Dr. K. H. Takemura.

(4) All melting points are corrected.

(5) Pl. A. Plattner and J. Pataki, *Helv. Chim. Acta*, **26**, 1241 (1943).