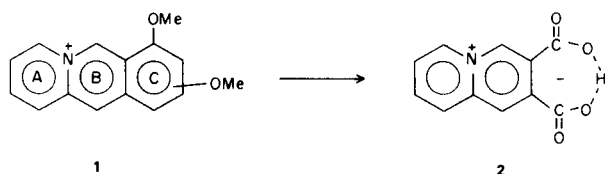


Derivatives of Dibenzo[*a,f*]quinolizinium Ion (1)

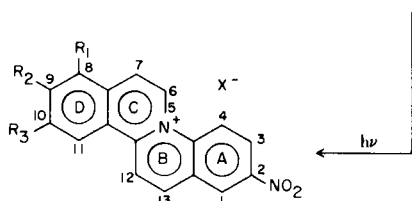
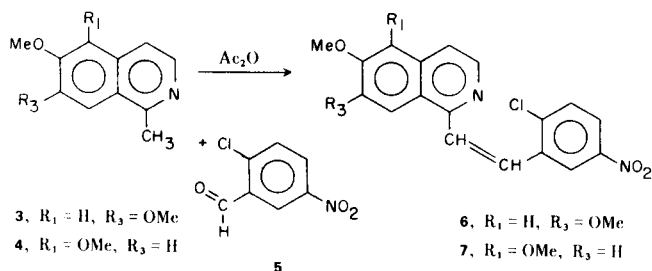
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It has been shown (2) that the nitric acid oxidation of acridizinium derivatives (1) having alkoxy groups in ring C leads to the betaine (2) of 2,3-dicarboxyquinolizinium hydroxide.



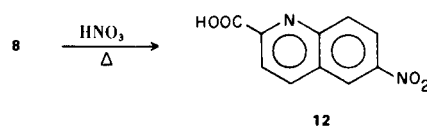
It seemed possible that the oxidation of a suitably substituted dibenzo[*a,f*]quinolizinium derivative (e.g., 8) might lead to the destruction of ring D leaving a dicarboxylic acid (or the betaine) which might serve as an intermediate in an azasteroid synthesis. The required 9-, 10- and 8,9-dimethoxy-2-nitrodibenzo[*a,f*]quinolizinium salts (8 and 9) were prepared by a photochemical method described earlier. The modification selected involved the condensation of the 1-methylisoquinoline derivative (3 or



- 8, $R_1 = \text{H}, R_2 = R_3 = \text{OMe}$
9, $R_1 = R_2 = \text{OMe}, R_3 = \text{H}$
10, $R_1 = \text{H}, R_2 = R_3 = \text{OAc}$
11, $R_1 = R_2 = \text{OH}, R_3 = \text{H}$

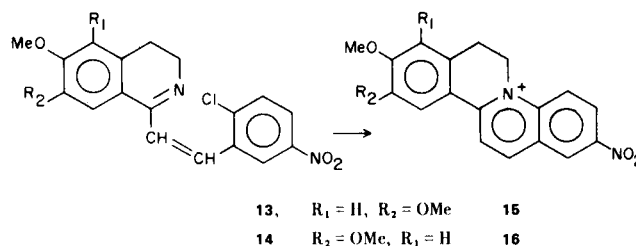
4) with 2-chloro-5-nitrobenzaldehyde (5) with the expectation that irradiation of the dimethoxy-1-(2'-chloro-5'-nitro)-styrylisoquinolines (6 and 7) in benzene solution would give the dibenzoquinolizinium salts (8 and 9) directly and in good yield. A further possibility of importance was that the nitro group, which occupies what would be termed position 3 in the steroid numbering system might be replaced by hydroxyl *via* reduction and diazotization.

Oxidation of 9,10-dimethoxy-2-nitrodibenzo[*a,f*]quinolizinium chloride (8) with nitric acid had the disappointing result that both rings D and C were destroyed and 6-nitroquinoline-2-carboxylic acid (12) was isolated. The struc-



ture of 12 was established by decarboxylation to yield 6-nitroquinoline. Milder oxidation methods were tried on 8 as well as the 9,10-diacetoxy derivative 10, but the mixtures obtained were not promising. Not enough of the 8,9-dimethoxy-2-nitrodibenzo[*a,f*]quinolizinium chloride (9) or the 8,9-dihydroxy analog (11) was prepared to permit adequate study of its oxidation.

An interesting discovery made during the course of this work was that 3,4-dihydro-1-methylisoquinolines condense with 2-chloro-5-nitrobenzaldehyde even more readily than do the fully aromatic counterparts (3 and 4) and the resulting 3,4-dihydro-1-(2'-chloro-5'-nitro)styrylisoquinolines 13 and 14 cyclize readily in refluxing ethyl acetate affording good yields of the 2-nitro-6,7-dihydrodibenzo[*a,f*]quinolizinium salts (15 and 16).



The elimination of the dehydrogenation step, required for the conversion of 1-methyl-3,4-dihydroisoquinolines (products of the Bischler-Napieralski reaction (4) to the aromatic isoquinoline derivative, will not only make the tetracyclic system more readily available, but will permit introduction of substituents not compatible with the usual dehydrogenation procedure.

EXPERIMENTAL

6,7-Dimethoxy-1-(2'-chloro-5'-nitro)styrylisoquinoline (6).

A mixture containing 5.5 g. of 2-chloro-5-nitrobenzaldehyde (5) (5), 6.1 g. of 1-methyl-6,7-dimethoxyisoquinoline (3) (6) and 8.2 g. of acetic anhydride was heated on a steam bath for 2 hours. The precipitate which formed was collected and recrystallized from benzene as yellow needles, m.p. 157-159°, yield 9.6 g. (86%); u.v. (ethanol) 237 μ (log ϵ , 4.58), 264 (4.54), 360 (4.11).

Anal. Calcd. for $C_{19}H_{15}ClN_2O_4$: C, 61.54; H, 4.08; N, 7.56. Found: C, 61.34; H, 4.26; N, 7.69.

1-Methyl-5,6-Dihydroisoquinoline (4).

The dehydrogenation of 1-methyl-5,6-dimethoxy-3,4-dihydroisoquinoline was carried out essentially as reported except that the melting point of the product (4) was found to be 99-100° instead of 93° (7).

Anal. Calcd. for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89. Found: C, 70.97; H, 6.51; N, 7.19.

5,6-Dimethoxy-1-(2'-chloro-5'-nitro)styrylisoquinoline (7).

The reaction of 4 with 5 was carried out essentially as in the preparation of 6 except that heating was continued for only 15 minutes and the product was crystallized from benzene-petroleum ether, m.p. 231-233° dec., yield 80%. The analytical sample, m.p. 235-236° was crystallized from acetonitrile; u.v. (ethanol) 210 μ (log ϵ , 4.54), 237 (4.59), 285 (4.59), and 345 (4.16).

Anal. Calcd. for $C_{19}H_{15}ClN_2O_4$: C, 61.54; H, 4.08; N, 7.56. Found: C, 61.45; H, 4.19; N, 7.51.

9,10-Dimethoxy-2-nitrobenzo[*a,f*]quinolizinium (8) chloride.

A solution of 2.0 g. of 6 in 430 ml. of thiophene-free benzene was irradiated for 39 hours using a 450 w Hanover water-cooled ultraviolet source with a Pyrex filter. The yellow precipitate 1.7 g. (85%) decomposed at 320° but did not melt below 360°. It was recrystallized from ethanol; u.v. (ethanol) 223 μ (log ϵ , 4.50), 281 (4.64), 323 (4.30), 416 (4.36).

Anal. Calcd. for $C_{19}H_{15}ClN_2O_4 \cdot 1.5H_2O$: C, 57.35; H, 4.56; N, 7.04. Found: C, 57.51; H, 4.42; N, 6.92.

8,9-Dimethoxy-2-nitrobenzo[*a,f*]quinolizinium (9) Perchlorate.

Irradiation of 1.0 g. of 7 was carried out for 60 hours essentially as in the preparation of 8. The product, m.p. 177° dec., obtained in 80% yield, was converted into the perchlorate m.p. 235° dec., for analysis; u.v. (ethanol) 218 μ (log ϵ , 4.51) 264 (4.34), 270 (4.34), 316 (4.57), 375 (4.28), 392 (4.41).

Anal. Calcd. for $C_{19}H_{15}ClN_2O_8$: C, 52.48; H, 3.48; N, 6.44. Found: C, 52.49; H, 3.66; N, 6.30.

6-Nitroquinoline-2-carboxylic acid (12) by Oxidation of 8.

Six g. of 8, X = Cl was mixed with 75 ml. of 12M nitric acid and heated on a steam bath for 24 hours. Upon dilution of the solution with water 2.8 g. of clear yellow needles was obtained. Recrystallization from acetonitrile afforded 1.2 g. (34%) of yellow

needles, m.p. 219-220°; u.v. (ethanol) 215 μ (log ϵ , 4.44), 253 (4.32), and 293 (4.08).

Anal. Calcd. for $C_{10}H_6N_2O_4$: C, 55.05; H, 2.77; N, 12.84. Found: C, 54.75; H, 2.82; N, 13.15.

A sample of the acid was mixed with an equal weight of copper and the mixture heated in a metal bath at 240° for several hours. The product which sublimed from the mixture was recrystallized from hexane as tan needles, m.p. 149-150° and was shown to be 6-nitroquinoline by mixture melting point with an authentic sample.

9,10-Diacetoxy-2-nitrodibenzo[*a,f*]quinolizinium (10) Bromide.

A suspension of 1 g. of 8, X = Cl in 20 ml. of 48% hydrobromic acid was stirred magnetically and refluxed under a nitrogen atmosphere. The mixture was heated for 2 hours during which the solid dissolved and then a green precipitate was formed. The precipitate of 0.8 g. was collected and 0.5 g. was acetylated by refluxing it for 0.5 hour in a mixture of 5 ml. of glacial acetic acid and 5 ml. of acetic anhydride. The red solid which crystallized on cooling was collected and recrystallized from methanol-ethyl acetate, m.p. 268° dec.; i.r. max. 5.7 μ (carbonyl); u.v. (ethanol) 220 μ (log ϵ , 4.44), 293 (4.59), 356 (3.97), 375 (4.13), 394 (4.23), 464 (2.81).

Anal. Calcd. for $C_{21}H_{15}BrN_2O_6 \cdot 0.5H_2O$: C, 52.51; H, 3.36; N, 5.83. Found: C, 52.13; H, 3.23; N, 5.51.

8,9-Dihydroxy-2-nitrodibenzo[*a,f*]quinolizinium (11) Bromide.

A suspension of 9, X = Cl in 20 ml. of 48% hydrobromic acid was refluxed under nitrogen as in the case of the isomer 8. The brown solid formed 1.0 g., m.p. > 360°, was recrystallized from methanol-ethyl acetate; u.v. (ethanol) 222 μ (log ϵ , 4.34), 237 (4.31), 278 (4.48), 325 (4.16), 425 (4.16), 457 (4.08).

Anal. Calcd. for $C_{17}H_{11}BrN_2O_4 \cdot 0.5H_2O$: C, 51.53; H, 3.05; N, 7.07. Found: C, 51.53; H, 3.25; N, 6.73.

6,7-Dimethoxy-3,4-dihydro-1-(2'-chloro-5'-nitro)styrylisoquinoline (13).

A solution of 2.4 g. of 1-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline (5) and 2.2 g. of 2-chloro-5-nitrobenzaldehyde (5) in benzene was allowed to stand at room temperature. A precipitate formed after 10 minutes, but the mixture was allowed to stand for several hours. The precipitate was collected affording 4.4 g. (100%) m.p. 137° dec. The analytical sample was obtained as yellow prisms m.p. 141° dec., from ethyl acetate; u.v. (ethanol) 226 μ (log ϵ , 4.17), 271 (3.98), 350 (3.03).

Anal. Calcd. for $C_{19}H_{17}ClN_2O_4 \cdot H_2O$: C, 58.39; H, 4.90; N, 7.17. Found: C, 58.60; H, 4.92; N, 6.94.

5,6-Dimethoxy-3,4-dihydro-1-(2'-chloro-5'-nitro)styrylisoquinoline (14).

To a solution of 0.55 g. of 2-chloro-5-nitrobenzaldehyde and 0.60 g. of 1-methyl-3,4-dihydro-5,6-dimethoxyisoquinoline in 5 ml. of benzene 0.2 g. of acetic anhydride was added and the mixture allowed to stand at room temperature for an hour and at refrigerator temperature overnight. The product, 0.4 g. (39%) m.p. 174° dec., could be rapidly recrystallized from ethyl acetate m.p. 180° dec.; u.v. (ethanol) 210 μ (log ϵ , 4.56), 268 (4.48) and 408 (4.09).

Anal. Calcd. for $C_{19}H_{17}ClN_2O_4$: C, 61.21; H, 4.60. Found: C, 60.87; H, 4.73.

9,10-Dimethoxy-6,7-dihydro-2-nitrodibenzo[*a,f*]quinolizinium Chloride (15).

A solution of 0.4 g. of 13 in 250 ml. of ethyl acetate was refluxed on a steam bath for 6 hours. The reddish precipitate, m.p. 205° dec., was recrystallized from ethanol; u.v. (ethanol) 217

$m\mu$ ($\log \epsilon$, 4.50), 264 (4.30), 301 (4.22) and 430 (4.29).

Anal. Calcd. for $C_{19}H_{17}ClN_2O_4 \cdot H_2O$: C, 58.39; H, 4.90; N, 7.17. Found: C, 58.70; H, 5.09; N, 6.77.

The perchlorate crystallized from acetone-acetonitrile as red prisms m.p. 278° dec.

Anal. Calcd. for $C_{19}H_{17}ClN_2O_8$: C, 52.24; H, 3.92; N, 6.42. Found: C, 52.24; H, 4.00; N, 6.46.

8,9-Dimethoxy-6,7-dihydro-2-nitrodibenzo[*a,f*]quinolizinium Chloride (**16**).

The cyclization of **14** was carried out in quantitative yield essentially as described for **13**, m.p. 220° dec., u.v. (ethanol) 212 $m\mu$ ($\log \epsilon$, 4.56), 260 (4.36), 299 (4.14) and 407 (4.54).

Anal. Calcd. for $C_{19}H_{17}ClN_2O_4 \cdot H_2O$: C, 58.39; H, 4.90; N, 7.17. Found: C, 58.33; H, 4.86; N, 7.11.

The perchlorate crystallized from ethanol as yellow needles, m.p. 287° dec.

Anal. Calcd. for $C_{19}H_{17}ClN_2O_8$: C, 52.24; H, 3.92; N, 6.42. Found: C, 52.01; H, 4.05; N, 6.22.

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