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A Direct Synthesis of 4-Azanaphthoquinones-1,2[1]

L. R. MORGAN, JR., AND R. J. SCHUNIOR

Department of Pharmacology, Louisiana State University, School of Medicine, New Orleans, Louisiana

AND J. H. BOYER

American Chemical Society, Petroleum Research Fund, Washington, District of Columbia

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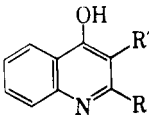
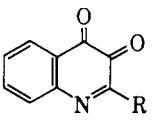
The difficulty encountered in the attempt to prepare azabenzoquinones[2] by the oxidation of hydroxy- and aminopyridones[3] suggested that fusion of a benzene ring to either an *o*- or *p*-azabenzoquinone might increase their stability. The reported synthesis and stability of 4-azanaphthoquinone-1,2 (IVa)[4] prompted an investigation of the chemistry of azanaphthoquinones. The present paper describes the preparation of two 4-azanaphthoquinones-1,2, IVa and IVb.



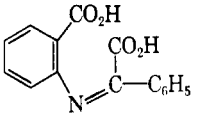


IVa. R = H
b. R = CH_3

Ia. R = R′ = H
b. R = CH_3, R′ = H
c. R = C_6H_5, R′ = H

IIa. R = H, R′ = CHO
b. R = CH_3, R′ = CHO
c. R = C_6H_5, R′ = CHO

IIIa. R = H, R′ = OH
b. R = CH_3, R′ = OH
c. R = C_6H_5, R′ = OH



V

The synthesis of IVa and IVb now reported utilizes the extension of the Reimer–Tiemann reaction to hydroxyquinolines. This approach finds analogy in the observation of Bobranski[5] that 4-hydroxyquinoline and 4-hydroxyquinaldine are formylated with sodium hydroxide and chloroform. Unfortunately a rigid structure proof of the products was not provided in either case.

Formylation of Ia, b, c under Bobranski's conditions proceeded as desired with formation of 3-formyl-4-hydroxyquinolines, IIa,b,c, in good yields. 3,4-Dihydroxyquinoline (IIIa) and 3,4-dihydroxyquinaldine (IIIb) were obtained from Dakin oxidations of IIa and IIb with sodium hydroxide and hydrogen peroxide in satisfactory yields. Oxidation of IIIa and IIIb was accomplished with silver oxide and/or chromium trioxide. The products have been assigned the structure of 4-azanaphthoquinone-1,2 (IVa) and 3-methyl-4-azanaphthoquinone-1,2 (IVb), respectively. Condensation of the azaquinones with *o*-phenylenediamine gave the corresponding phenazines supporting the initial assignments of the formyl group in IIa and IIb.

In sharp contrast to the foregoing results, the Dakin oxidation of 2-phenyl-3-formyl-4-hydroxyquinoline (IIc) with sodium hydroxide and hydrogen peroxide to 2-phenyl-3,4-dihydroxyquinoline (IIIc) was unsuccessful. The major product was the anthranil of phenylglyoxylic acid (V) whose structure was confirmed by hydrolysis to phenylglyoxylic acid. Apparently in addition to the Dakin oxidation of the formyl group in IIc a Baeyer–Villiger transformation occurs with oxidation of an intermediate peroxide and ring fission. All attempts to stop the reaction at the dihydroxy stage were unsuccessful.

Experimental[6]

Preparation of the 4-Hydroxyquinolines (Ia–c).—4-Hydroxyquinaldine,[7] 2-phenyl-4-hydroxyquinoline,[8] and 4-hydroxyquinoline[9] were prepared according to the literature cited.

Preparation of the 3-Formyl-4-hydroxyquinolines (IIa–c).—3-Formyl-4-hydroxyquinoline[5] and 3-formyl-4-hydroxyquinaldine[10] were previously prepared.

A mixture of 2-phenyl-4-hydroxyquinoline (2.87 g., 0.013 mole), 2 g. of powdered sodium hydroxide, and 2 ml. of chloroform was heated at 50° for a few minutes and 3 ml. of water added. The slurry was gently refluxed for 6 hr. with 2 ml. of chloroform being added at 2-hr. intervals. The excess chloroform was removed *in vacuo* and the resulting slurry filtered. The dried solid was extracted twice with 20–30 ml. of hot water and the washings combined with the original filtrate. Acidification with glacial acetic acid afforded a yellow suspension which precipitated as a yellow sirup that solidified upon standing. Several recrystallizations from ethanol afforded yellow needles of 2-phenyl-3-formyl-4-hydroxyquinoline, m.p. 250–252°, 1.2 g. (37%).

Anal. Calcd. for $C_{16}H_{11}NO_2$: C, 77.09; H, 4.45; N, 5.63. Found: C, 77.27; H, 4.52; N, 5.57.

The aldehyde formed a 2,4-dinitrophenylhydrazone which recrystallized from ethyl acetate and ethanol as red needles, m.p. 275–277.5° dec.

Anal. Calcd. for $C_{22}H_{15}N_5O_5$: C, 61.54; H, 3.52; N, 16.31. Found: C, 61.27; H, 3.45; N, 16.41.

General Procedure for the Dakin Oxidation of 3-Formyl-4-hydroxyquinolines (IIa–b).—To a solution of 0.007 mole of the 3-formyl-4-hydroxyquinolines in 7 ml. of 1 *N* sodium hydroxide, 9.5 g. of 3% hydrogen peroxide was added in one portion and allowed to stand overnight at room temperature. A color change from deep orange to yellow was accompanied by an exothermic reaction. Upon cooling to room temperature the dihydroxyquinolines could be isolated.

3,4-Dihydroxyquinoline recrystallized from 95% ethanol as yellow microcrystals, m.p. 222–227° dec., 18% yield.

Anal. Calcd. for $C_9H_7NO_2$: C, 67.07; H, 4.38; N, 8.69. Found: C, 67.13; H, 4.21; N, 8.75.

3,4-Dihydroxyquinaldine recrystallized from 95% ethanol as a pale yellow powder, m.p. 275–281° dec., 49% yield.

(1) Part of this work was carried out in the Department of Chemistry, Tulane University, New Orleans, La.

(2) In the present study, azaquinones designates nitrogen as a member of the quinone ring.

(3) J. H. Boyer and S. Kruger, *J. Am. Chem. Soc.*, **79**, 3552 (1957).

(4) M. Passerini, T. Bonciani, and N. Di Gioia, *Gazz. chim. ital.*, **61**, 959 (1931).

(5) B. Bobranski, *Chem. Ber.*, **69**, 1113 (1888).

(6) Semimicro analyses by Alfred Bernhardt Microanalytisches Laboratorium, Max Planck Institute, Mülheim (Ruhr), Germany. Melting points are uncorrected.

(7) G. A. Reynolds and C. R. Hauser, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 593.

(8) R. C. Fuson and D. M. Burness, *J. Am. Chem. Soc.*, **61**, 2890 (1939).

(9) R. G. Gould, Jr., and W. A. Jacobs, *ibid.*, **61**, 2890 (1939).

(10) M. Conrad and L. Limpach, *Chem. Ber.*, **21**, 1965 (1888).

Anal. Calcd. for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 7.99. Found: C, 68.66; H, 4.99; N, 7.85.

4-Azanaphthoquinone-1,2 (IVa).—To a solution of 0.10 g. (0.62 mmole) of 3,4-dihydroxyquinoline in 10 ml. of glacial acetic acid at 20°, a suspension of 0.5 g. of chromium trioxide in 10 ml. of glacial acetic acid was added slowly. The mixture was warmed on a steam bath to 40° and allowed to stand at room temperature overnight. The dark green mixture was diluted with 50 ml. of water and the pale yellow microcrystals of 4-azanaphthoquinone-1,2 that separated were collected and recrystallized from methanol or dioxane, 45 mg. (45%), dec. > 285°.[4]

Anal. Calcd. for $C_9H_5NO_2$: C, 67.92; H, 3.17; N, 8.80. Found: C, 67.98; H, 3.25; N, 8.62.

A phenazine derivative of IVa was prepared from *o*-phenylenediamine dihydrochloride and sodium acetate in glacial acetic acid and recrystallized from xylene as a red powder, dec. > 300°.

Anal. Calcd. for $C_{15}H_9N_3$: C, 77.90; H, 3.92; N, 18.17. Found: C, 77.98; H, 4.17; N, 17.90.

3-Methyl-4-azanaphthoquinone-1,2 (IVb).—A solution of 0.11 g. (0.0062 mole) of 3,4-dihydroxyquinaldine in 50 ml. of anhydrous methanol was shaken with 4 g. of dry silver oxide and 15 g. of anhydrous sodium sulfate for 10 min. and filtered. The yellow filtrate was evaporated to dryness under reduced pressure at room temperature and the yellow residue collected. Four recrystallizations from 95% ethanol afforded yellow plates of 3-methyl-4-azanaphthoquinone-1,2, 46 mg. (42%), m.p. 261–265° dec. Elemental analysis was not obtained due to unstability.

3-Methyl-4-azanaphthoquinone-1,2 upon treatment with *o*-phenylenediamine dihydrochloride and sodium acetate in glacial acetic acid afforded the corresponding phenazine, which recrystallized from benzene as red plates, m.p. 321–322.5° dec.

Anal. Calcd. for $C_{16}H_{11}N_3$: C, 78.35; H, 4.52; N, 17.13. Found: C, 78.42; H, 4.39; N, 17.41.

Dakin Oxidation of 2-Phenyl-3-formyl-4-hydroxyquinoline (IIIc).—To a solution of 0.42 g. (0.0017 mole) of 2-phenyl-3-formyl-4-hydroxyquinoline in 1.7 ml. of 1 *N* sodium hydroxide, 2.31 g. of 3% hydrogen peroxide was added in one portion. A color change from deep orange to pale yellow was accompanied by an exothermic reaction. Upon cooling to room temperature the disodium salt of the anthranil of phenylglyoxylic acid (V) precipitated which recrystallized from 95% ethanol as yellow microcrystals, dec. > 350°, 380 mg. (72%).

Anal. Calcd. for $C_{15}H_9NO_4Na_2$: C, 57.51; H, 2.90; N, 4.47. Found: C, 57.28; H, 3.11; N, 4.77.

Refluxing V with an excess of 2,4-dinitrophenylhydrazine in ethanol (10% hydrochloric acid) afforded the 2,4-dinitrophenylhydrazone of phenylglyoxylic acid, m.p. and mixture m.p. 196–197°.

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Hydroboration of Diphenylacetylene

ALFRED HASSNER AND BERNARD H. BRAUN

Department of Chemistry, University of Colorado, Boulder, Colorado

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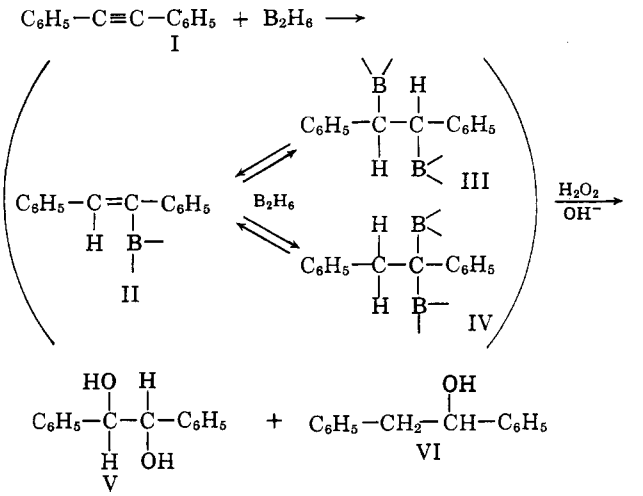
Addition of diborane to olefins (hydroboration) followed by oxidative workup has been shown to be a reaction of general utility in the synthesis of alcohols.[1] The reaction is stereospecific—*i.e.*, *cis* addition of the elements of water, and the least substituted alcohol is generally formed.[1a,b]

(1)(a) H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, **22**, 1136 (1957); H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **81**, 247 (1959) and subsequent papers; for a review see H. C. Brown, *Tetrahedron*, **12**, 117 (1961). (b) A. Hassner and C. Pillar, *J. Org. Chem.*, **27**, 2914 (1962).

We were interested in applying this hydration scheme to the formation of *d,l* or *erythro* diols from acetylenes. Terminal acetylenes have been reported to yield aldehydes on hydroboration.[2,3] When we applied the reaction to diphenylacetylene (I) we found that in addition to the expected *d,l*-dihydrobenzoin (V) (37%), a large amount (40%) of 1,2-diphenylethanol (VI) was also formed. Small amounts of *trans*-stilbene and of desoxybenzoin were also found. No *meso*-dihydrobenzoin nor any rearranged 1,1-diphenyl-1,2-ethanediol was detected. The starting diphenylacetylene was virtually free of any stilbene as shown by infrared studies.



It is apparent that 1,2-diphenylethanol (VI) cannot result by a normal path from either of the expected intermediates II, III, or IV. Desoxybenzoin could be formed in the reaction on oxidation of intermediate II or IV and hydrolysis. To ensure that, at the time of formation of desoxybenzoin, diborane or any B—H compound needed to effect reduction to VI will have been destroyed, acetone was added prior to oxidative work-up; this did not affect the product distribution. Brown and Zweifel[3] also observed predominant formation of monoalcohols in the hydroboration of acetylenes and attributed these results to hydrolytic cleavage of an intermediate of type IV.[4] Alternatively, borane-induced elimination of the elements of >B—B< from intermediate III, followed by hydroboration of the resulting stilbene, could lead to alcohol VI and at the same time explain the isolation of a small amount of *trans*-stilbene. Abnormal products of a different nature were reported in the hydroboration of di-*tert.*-butyl-

(2) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **81**, 1512 (1959).

(3) H. C. Brown and G. Zweifel, *ibid.*, **83**, 3834 (1961).

(4) One also could envisage a process of internal hydride transfer in intermediate II, as pictured: