[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

An Extension of the Diels–Reese Reaction[1]

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RECEIVED OCTOBER 17, 1955

The adduct from dimethyl acetylenedicarboxylate and 4,4′-dimethylhydrazobenzene yielded no indole derivative under the conditions of the Diels–Reese reaction but did give, by heating in α-picoline, 2-hydroxy-3-(*p*-toluino)-4-carbomethoxy-6-methylquinoline. The latter was degraded to 2,3-dihydroxy-6-methylquinoline. The adduct from dimethyl acetylenedicarboxylate and 4,4′-dichlorohydrazobenzene gave both dimethyl 5-chloroindole-2,3-dicarboxylate and 2-hydroxy-3-(*p*-chloranilino)-4-carbomethoxy-6-chloroquinoline under suitable conditions. The latter was degraded to 2,3-dihydroxy-6-chloroquinoline. The adduct from dimethyl acetylenedicarboxylate and 4-acetoxyhydrazobenzene did not yield any indole derivative but did produce, by heating in α-picoline, 2-hydroxy-3-anilino-4-carbomethoxy-6-acetoxyquinoline. The latter was degraded to the hitherto unknown 2,3,6-trihydroxyquinoline which was also prepared by an independent synthesis.

Diels and Reese[3] found that dimethyl acetylenedicarboxylate and hydrazobenzene react in warm methanol to form a 1:1 adduct which could be transformed under suitable conditions to three types of heterocyclic compounds. In glacial acetic acid, the adduct yielded 1,2-diphenyl-3-carbomethoxy-5-pyrazolone (III), in xylene it gave dimethyl indole-2,3-dicarboxylate (IV, R = R¹ = H) while in pyridine it afforded 2-hydroxy-3-anilino-4-carbomethoxyquinoline (V, R = R¹ = H). V (R = R¹ = H) was degraded[4] to 2,3-dihydroquinoline (VII, R = R¹ = H) by decarboxylation of the derived acid (VI, R = R¹ = H) followed by hydrolysis of the anilino group.

We have completely substantiated this remarkable series of reactions reported by Diels and Reese and have now extended the above reactions to three substituted hydrazobenzenes. The formation of the corresponding pyrazolones, however, has not been studied since they are readily prepared by simpler procedures. The hydrazobenzenes used were the 4,4′-dimethyl-, the 4,4′-dichloro- and the 4-acetoxy-. All formed adducts readily with dimethyl acetylenedicarboxylate in good yield.

The adduct from 4,4′-dimethylhydrazobenzene when heated in α-picoline gave the expected 2-hydroxy-3-(*p*-toluino)-4-carbomethoxy-6-methylquinoline (V, R = R¹ = CH_3) which on saponification gave the free acid (VI, R = R¹ = CH_3). VI (R = R¹ = CH_3) on hydrolysis and decarboxylation produced 2,3-dihydroxy-6-methylquinoline (VII, R = CH_3). This same adduct when heated in xylene did not give the corresponding indole, however, but only the quinoline derivative listed above V (R = R¹ = CH_3).

The adduct from 4,4′-dichlorohydrazobenzene gave the expected products. In α-picoline, it yielded 2-hydroxy-3-(*p*-chloroanilino)-4-carbomethoxy-6-chloroquinoline (V, R = R¹ = Cl) which was saponified to the free acid (VI, R = R¹ = Cl), which, in turn, was hydrolyzed and decarboxylated with hydriodic acid (neither hydrochloric nor hydrobromic acids were effective) to the corresponding 2,3-dihydroxy-6-chloroquinoline (VII, R = Cl). The adduct readily gave dimethyl 5-chloroindole-2,3-dicarboxylate (IV, R = Cl) when heated under reflux in xylene.

Whereas symmetrically substituted hydrazobenzenes can give only unambiguous heterocyclic products under the conditions of the Diels–Reese reaction, a monosubstituted reagent could give two possible products or a mixture of them. When 4-acetoxyhydrazobenzene (I, R = $OCOCH_3$, R¹ = H) was treated with dimethyl acetylenedicarboxylate, only a single adduct was isolated. This adduct when heated in α-picoline gave what proved to be 2-hydroxy-3-anilino-4-carbomethoxy-6-acetoxyquinoline (V, R = $OCOCH_3$, R¹ = H). None of the other possible isomer, 2-hydroxy-3-(*p*-acetoxyanilino)-4-carbomethoxyquinoline (V, R = H, R¹ = $OCOCH_3$), was found. The degradation of V (R = $OCOCH_3$, R¹ = H) gave aniline (VIII, R¹ = H) and the hitherto unknown 2,3,6-trihydroxyquinoline (VII, R = OH), which, to our knowledge, is the first trihydroxyquinoline of unambiguous structure. Had the original quinoline been V (R = H, R¹ = $OCOCH_3$), the degradation products would have been the previously reported[3] 2,3-dihydroxyquinoline (VII, R = H) and *p*-aminophenol (VIII, R¹ = OH).

As confirmation of the structure of the trihydroxyquinoline, it was prepared by a new, independent synthesis. To test this synthetic method, 2,3-dihydroxyquinoline was prepared by reaction of 2-aminobenzaldehyde (IX, R = H) with chloroacetic anhydride to give 2-(N-chloroacetamino)-benzaldehyde (X, R = H) which was readily converted by heating under reflux with methanolic aqueous potassium hydroxide to 2,3-dihydroxyquinoline (XI, R = H) in good yield.

From 5-methoxy-2-aminobenzaldehyde (IX, R = OCH_3), the corresponding N-chloroacetamino derivative (X, R = OCH_3) was formed, which on ring closure gave 2,3-dihydroxy-6-methoxyquinoline (XI, R = OCH_3). Demethylation of XI (R = OCH_3) gave 2,3,6-trihydroxyquinoline (XI, R = OH) which was identical with that formed from 4-acetoxyhydrazobenzene and dimethyl acetylenedicarboxylate.

The adduct from 4-acetoxyhydrazobenzene and dimethyl acetylenedicarboxylate when heated under reflux in xylene did not yield any indole derivative, although either dimethyl indole-2,3-dicarboxylate (IV, R = H) or the 5-acetoxy derivative (IV, R = $OCOCH_3$) would be expected. Refluxing of the adduct in xylene, toluene, *m*-diethylbenzene or tetralin produced only amorphous or tarry material. Similarly, heating of the components of the adduct under reflux in xylene produced no indole derivative.

(1) Abstracted from a thesis submitted in partial fulfillment of the requirements for the Ph.D. degree at the Massachusetts Institute of Technology by Joseph Bornstein.

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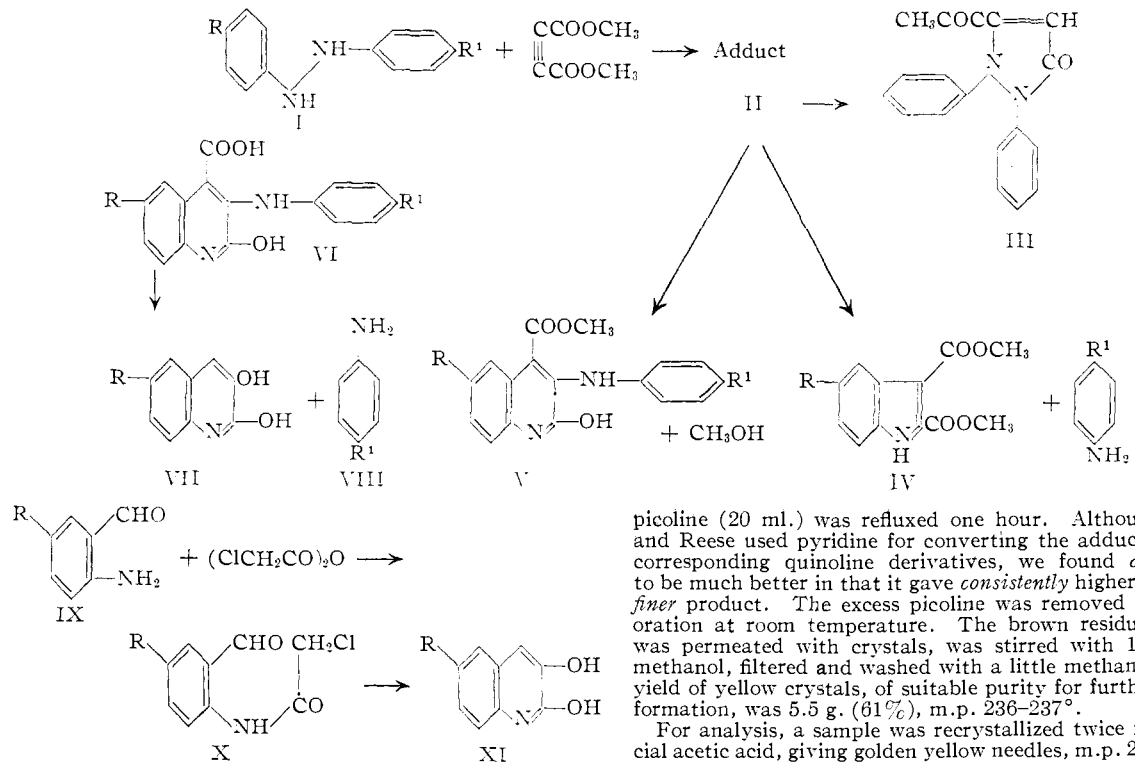
(3) O. Diels and J. Reese, *Ann.*, **511**, 168 (1934).

(4) O. Diels and J. Reese, *ibid.*, **519**, 147 (1935).



Experimental[5]

Preparation of Adducts. A. Adduct of 4,4'-Dimethylhydrazobenzene.—A mixture of freshly prepared 4,4'-dimethylhydrazobenzene[6] (6.5 g., 0.031 mole), methanol (20 ml.) and dimethyl acetylenedicarboxylate (5.5 g., 0.038 mole) was heated under reflux. Within a minute, the solid dissolved to form an orange-red solution which boiled spontaneously for four minutes. The reaction mixture was heated under reflux for an additional 90 minutes. After standing in the ice-box overnight, the mixture had set to a yellow mash which was filtered and washed with 5 ml. of cold ether. The yield of light yellow powder, suitable for further use without additional purification, was 7.1 g. (66%), m.p. 138–140° dec. uncor. (recorded[4] m.p. 146°).

B. Adduct of 4,4'-Dichlorohydrazobenzene.—Prepared as above from 4,4'-dichlorohydrazobenzene[7] (5.0 g., 0.02 mole), dimethyl acetylenedicarboxylate (2.9 g., 0.02 mole) and methanol (8 ml.) which gave when washed with petroleum ether (25 ml.) 6.0 g. of adduct (77%).

For analysis, the adduct was recrystallized twice from methanol and dried over sulfuric acid at 2 mm. for three hours at room temperature, m.p. 135.5–136° dec.

Anal. Calcd. for $C_{18}H_{16}O_4N_2Cl_2$: C, 54.71; H, 4.08; N, 7.09; Cl, 17.94. Found: C, 54.62; H, 4.12; N, 7.26; Cl, 17.81.

C. Adduct from 4-Acetoxyhydrazobenzene.—Prepared as above from 4-acetoxyhydrazobenzene[8] (60.0 g., 0.25 mole), dimethyl acetylenedicarboxylate (36.0 g., 0.26 mole) and methanol (60 ml.) which gave, after washing with ether, 80 g. of adduct (83%).

For analysis, a sample was recrystallized twice from methanol, m.p. 164–165°.

Anal. Calcd. for $C_{20}H_{20}O_6N_2$: C, 62.49; H, 5.25; N, 7.29; mol. wt., 384.4. Found: C, 62.29; H, 5.37; N, 7.33; mol. wt., 417.7 (cryoscopic, benzene).

2-Hydroxy-3-(*p*-toluino)-4-carbomethoxy-6-methylquinoline (V, R = R¹ = CH₃).—A solution of the adduct from 4,4'-dimethylhydrazobenzene (10.0 g., 0.028 mole) in α-picoline (20 ml.) was refluxed one hour. Although Diels and Reese used pyridine for converting the adducts to the corresponding quinoline derivatives, we found α-picoline to be much better in that it gave *consistently* higher yields of *finer* product. The excess picoline was removed by evaporation at room temperature. The brown residue, which was permeated with crystals, was stirred with 10 ml. of methanol, filtered and washed with a little methanol. The yield of yellow crystals, of suitable purity for further transformation, was 5.5 g. (61%), m.p. 236–237°.

For analysis, a sample was recrystallized twice from glacial acetic acid, giving golden yellow needles, m.p. 237–238°.

Anal. Calcd. for $C_{19}H_{18}O_3N_2$: C, 70.83; H, 5.63; N, 8.70. Found: C, 71.15; H, 5.82; N, 8.56.

2-Hydroxy-3-(*p*-toluino)-4-carboxy-6-methylquinoline (VI, R = R¹ = CH₃).—Refluxing of 2-hydroxy-3-(*p*-toluino)-4-carbomethoxy-6-methylquinoline (4.0 g., 0.0124 mole) in a solution of potassium hydroxide (5.0 g., 0.009 mole) in 50 ml. of aqueous 50% ethanol for two hours gave on acidification 3.5 g. (91%) of yellow solid.

For analysis, a sample was recrystallized from glacial acetic acid as golden needles which began to decompose at 229° when a melting point determination was run.

Anal. Calcd. for $C_{18}H_{16}O_3N_2$: C, 70.15; H, 5.23; N, 9.08. Found: C, 70.15; H, 5.39; N, 9.30.

2,3-Dihydroxy-6-methylquinoline (VII, R = CH₃).—Crude 2-hydroxy-3-(*p*-toluino)-4-carboxy-6-methylquinoline (3.5 g., 0.0114 mole) was cautiously heated under reflux with a mixture of concentrated hydrochloric acid (35 ml.) and glacial acetic acid (35 ml.). The solid dissolved during the first hour with violent foaming due to the evolution of carbon dioxide to yield a clear, light red solution which was refluxed an additional three hours. The mixture, after dilution with 200 ml. of cold water and standing overnight in the refrigerator, deposited 1.9 g. (96%) of pink solid.

For analysis, a sample was recrystallized twice from aqueous 20% methanol (Norite) giving white, felted needles, m.p. 228–229°.

Anal. Calcd. for $C_{10}H_9O_2N$: C, 68.59; H, 5.18; N, 8.00. Found: C, 68.68; H, 5.40; N, 7.91.

Attempted Preparation of Dimethyl 5-Methylindole-2,3-dicarboxylate (IV, R = CH₃).—A suspension of the adduct from 4,4'-dimethylhydrazobenzene and dimethyl acetylenedicarboxylate (2.0 g., 0.0057 mole) in commercial xylene (4 ml.) was refluxed one hour. The brown solution on cooling deposited a yellow solid which was filtered and washed with methanol to give 1.1 g. (60%) of product. One recrystallization from glacial acetic acid gave small golden-yellow needles melting at 236–237°. A mixed melting point determination with 2-hydroxy-3-(*p*-toluino)-4-carbomethoxy-6-methylquinoline (V, R = R¹ = CH₃) made above showed no depression.

2-Hydroxy-3-(*p*-chloranilino)-4-carbomethoxy-6-chloroquinoline (V, R = R¹ = Cl).—A solution of the adduct from 4,4'-dichlorohydrazobenzene and dimethyl acetylenedicarboxylate (12.0 g., 0.030 mole) in α-picoline (36 ml.) was refluxed 70 minutes. The excess solvent was removed by evaporation at 65°. The residue which was permeated with

(5) All melting points are corrected, unless otherwise indicated. We are indebted to Dr. S. M. Nagy and his associates for elemental analyses.

(6) J. V. Janovsky, *Monatsh.*, **9**, 829 (1888).

(7) A. Calm and K. Heumann, *Ber.*, **13**, 1180 (1880).

(8) H. Goldschmidt and R. Brubacher, *ibid.*, **24**, 2309 (1891).

crystals was taken up in the minimum amount of boiling glacial acetic acid, treated with charcoal and filtered. The filtrate was diluted dropwise with water until a faint, permanent turbidity appeared, and was then kept at room temperature overnight. The precipitated solid was filtered, washed with 15 ml. of methanol and air-dried to give 8.0 g. (73%) of golden-yellow crystals, m.p. 284–285°.

For analysis, a sample was recrystallized from ethanol–water as small yellow prisms; the m.p. was unchanged.

Anal. Calcd. for $C_{17}H_{12}N_2O_3Cl_2$: C, 56.20; H, 3.33; N, 7.72; Cl, 19.52. Found: C, 56.47; H, 3.54; N, 7.72; Cl, 19.15.

2-Hydroxy-3-(*p*-chloroanilino)-4-carboxy-6-chloroquinoline (VI, R = R¹ = Cl).—The ester (V, R = R¹ = Cl) (1.4 g., 3.9 mmoles) was saponified by heating under reflux two hours with potassium hydroxide (1.3 g., 0.023 mole) in a mixture of 95% ethanol (5 ml.) and water (10 ml.). Acidification of the reaction mixture gave 1.1 g. (82%) of yellow crystals.

One recrystallization from glacial acetic acid gave the analytical sample as small yellow needles, m.p. 321–322° dec.

Anal. Calcd. for $C_{16}H_{10}O_3N_2Cl_2$: C, 55.03; H, 2.89; N, 8.02; Cl, 20.30. Found: C, 55.01; H, 2.95; N, 8.04; Cl, 20.00.

2,3-Dihydroxy-6-chloroquinoline (VII, R = Cl).—A mixture of 2-hydroxy-3-(*p*-chloranilino)-4-carboxy-6-chloroquinoline (1.3 g., 3.7 mmoles), hydriodic acid (16 ml., d. 1.7) and glacial acetic acid (10 ml.) was refluxed three hours. The mixture was diluted with 150 ml. of cold water and immediately a white solid deposited, 0.7 g. (95%). The compound was obtained after two recrystallizations from absolute ethanol as small needles, m.p. 303–304°, with sublimation. The compound gave a purple-red coloration with methanolic aqueous ferric chloride.

Anal. Calcd. for $C_9H_6O_2NCl$: C, 55.25; H, 3.09; N, 7.16; Cl, 18.12. Found: C, 55.26; H, 3.42; N, 7.19; Cl, 17.85.

Dimethyl 5-Chloroindole-2,3-dicarboxylate (IV, R = Cl).—The adduct from 4,4'-dichlorohydrazobenzene and dimethyl acetylenedicarboxylate (1.0 g., 0.0025 mole) was refluxed in commercial xylene (2 ml.) for 90 minutes. The orange-red solution on cooling set to a solid which was filtered and air-dried to give 0.5 g. (74%) of IV (R = Cl). The product was purified by boiling for five minutes with methanol (30 ml.), filtering from traces of 4,4'-dichlorazobenzene, treating the filtrate with charcoal, and diluting with water (20 ml.). After being refrigerated overnight, the solution gave white needles, m.p. 166.5–168°.

For analysis, a sample was crystallized from methanol as small, white needles, m.p. 168–168.5°.

Anal. Calcd. for $C_{12}H_{10}O_4NCl$: C, 53.85; H, 3.77; N, 5.24; Cl, 13.25. Found: C, 53.79; H, 3.73; N, 5.32; Cl, 13.44.

The vapors from a sample heated to dryness with aqueous potassium hydroxide gave a positive (red-violet coloration) pine splinter test, while a sample which was heated with concentrated sulfuric acid and then diluted with methanol gave a positive (red coloration) Ehrlich test.

The xylene filtrate from above was extracted with 10 ml. of dilute hydrochloric acid. The acid extract was made alkaline and extracted with three 10-ml. portions of ether. The combined ether extracts were dried over sodium sulfate and evaporated to give *p*-chloroaniline, m.p. 69–70°; recorded[9] m.p. 70°. The acetyl derivative melted at 179°; recorded[9] m.p. 179°.

2-Hydroxy-3-anilino-4-carbomethoxy-6-acetoxyquinoline (V, R = OCOCH₃, R¹ = H).—The adduct from 4-acetoxyhydrazobenzene and dimethyl acetylenedicarboxylate (18.0 g., 0.047 mole) and α-picoline (60 ml.) were refluxed for 80 minutes. The excess solvent was removed by evaporation at 65° and the brownish viscous residue stirred with methanol (10 ml.). The resulting crystals were filtered, washed with cold methanol (20 ml.) and digested for 20 minutes with methanol (50 ml.). After cooling and filtering, 11.5 g. (70%) of yellowish-green crystals, m.p. 256–257°, was obtained.

For analysis, a sample was recrystallized from methanol to give fine, yellowish-green needles which fluoresced bright green under ultraviolet light. The m.p. was unchanged.

Anal. Calcd. for $C_{19}H_{16}O_5N_2$: C, 64.77; H, 4.58; N, 7.95; sapon. equiv., 176.2. Found: C, 64.90; H, 4.55; N, 8.04; sapon. equiv., 173.5, 175.5.

2,6-Dihydroxy-3-anilino-4-carboxyquinoline (VI, R = OH, R¹ = H).—Heating of 2-hydroxy-3-anilino-4-carbomethoxy-6-acetoxyquinoline (10.0 g., 0.034 mole) under reflux in 20% aqueous potassium hydroxide (40 ml.) for 15 minutes followed by acidification gave the crude dihydroxy acid. Recrystallization from 50% methanol gave yellow needles (6.0 g., 72% of theory) which began to decompose when heated to 218°.

For analysis, the product was recrystallized from methanol from which it separated with one mole of solvent.

Anal. Calcd. for $C_{16}H_{12}O_4N\cdot CH_3OH$: C, 62.19; H, 4.91; N, 8.54. Found: C, 62.24; H, 5.04; N, 8.51.

2,3,6-Trihydroxyquinoline (VII, R = OH). A. From 2,6-Dihydroxy-3-anilino-4-carboxyquinoline (VI, R = OH, R¹ = H).—A mixture of VI (R = OH, R¹ = H) (2.0 g., 0.0068 mole), glacial acetic acid (2 ml.) and concentrated hydrochloric acid (6 ml.) was refluxed two hours. The filtered solution on dilution with 20 ml. of cold water deposited a light pink-colored solid which was filtered after being refrigerated overnight (1.1 g., 92%). The product was recrystallized from water containing charcoal to give white needles, m.p. 315–317° (dec., sublimation).

For analysis, a sample was purified to constant m.p. by crystallization successively from water and methanol using charcoal each time, m.p. 318–319° dec. after drying at 100° for two hours.

Anal. Calcd. for $C_9H_7O_3N$: C, 61.01; H, 3.99; N, 7.91. Found: C, 61.14; H, 4.03; N, 8.07.

The compound gave a positive Fehling test on warming, a silver mirror with Tollens reagent in the cold, and a deep blue color with aqueous ferric chloride.

An aqueous alkaline solution of the substance turned brownish-red on standing in air. An ethanolic solution of the quinoline fluoresced violet under ultraviolet light.

From the hydrochloric–acetic acid filtrate 0.4 g. (63%) of aniline was obtained, identified as its acetyl derivative, m.p. 113–114°; recorded 114°.

The trihydroxyquinoline was further characterized as the monoacetyl derivative obtained by treatment of the quinoline with a twenty-fold amount of acetic anhydride containing a trace of pyridine at 90° for two hours. Crystallized twice from aqueous 20% methanol (Norite) gave pink needles, m.p. 228–229°.

Anal. Calcd. for $C_{11}H_9O_4N$: N, 6.39. Found: N, 6.33.

B. From 5-Methoxy-2-nitrobenzaldehyde. 5-Methoxy-2-(N-chloroacetamino)-benzaldehyde (X, R = OCH₃).—To a boiling solution of ferrous sulfate heptahydrate (35.0 g., 0.13 mole) in 75 ml. of water was added 5-methoxy-2-nitrobenzaldehyde[10,11] (2.0 g., 0.011 mole) in the form of its bisulfite addition compound[12] (prepared by dissolving the aldehyde in 15 ml. of water containing 2.0 g. of sodium bisulfite). To the mixture was added in 5-ml. portions saturated aqueous sodium carbonate with vigorous stirring until a permanent alkaline reaction to litmus was observed. The black-colored mixture was boiled an additional five minutes and filtered hot. The ferric hydroxide cake was washed with two 25-ml. portions of water which were combined with the yellow filtrate and extracted three times with 200-ml. portions of ether. The ether extract was dried over anhydrous sodium sulfate and concentrated to 50 ml. To this solution was added chloroacetic anhydride (2.2 g., 0.013 mole) in 50 ml. of anhydrous ether. The reaction mixture was kept at room temperature overnight and the ether then removed under reduced pressure. The resulting solid was recrystallized from aqueous 80% methanol to give pale yellow felted needles, m.p. 136.5–137.5°; yield 1.1 g. (44% of theory, over-all).

Anal. Calcd. for $C_{10}H_{10}O_3NCl$: C, 52.79; H, 4.43; N, 6.16; Cl, 15.58. Found: C, 52.63; H, 4.56; N, 6.41; Cl, 15.66.

(9) Clarke, "Handbook of Organic Analysis," Edward Arnold and Co., London, 1926, p. 258.

(10) F. A. Mason and H. Jenkinson, *J. Chem. Soc.*, **127**, 1195 (1925).

(11) M. E. Smith, E. Elisberg and M. L. Sherrill, THIS JOURNAL, **68**, 1301 (1946).

(12) J. Tröger and C. Cohaus, *J. prakt. Chem.*, [2] **117**, 102 (1927).

2,3-Dihydroxy-6-methoxyquinoline (X, R = OCH_3).—To a stirred, refluxing solution of 1.0 g. (0.018 mole) of potassium hydroxide in 100 ml. of water was added dropwise over a ten-minute period, a solution of 5-methoxy-2-(N-chloracetylamino)-benzaldehyde (0.8 g., 0.0035 mole) in 20 ml. of hot *n*-propyl alcohol. The solution was refluxed and stirred for two hours and then concentrated to 30 ml. After treatment of the reaction mixture with charcoal followed by acidification with concentrated hydrochloric acid, a light tan solid separated which was filtered and washed with water; yield 0.5 g. (75%). One recrystallization from water with charcoal gave fine, white needles, m.p. 231–232°.

For analysis, the compound was recrystallized successively from aqueous 50% methanol and aqueous 20% methanol using charcoal each time, m.p. 228–230°.

Anal. Calcd. for $C_{10}H_9O_3N$: C, 62.82; H, 4.75; N, 7.32. Found: C, 62.64; H, 4.85; N, 7.45.

The compound gave an intense blue coloration with aqueous ferric chloride.

Acetylation of the crude quinoline (0.6 g.) with acetic anhydride (5 ml.) and pyridine (3 drops) at 90° for two hours gave, from aqueous 20% methanol, nearly white needles, m.p. 185–186°.

Anal. Calcd for $C_{12}H_{11}O_4N$: C, 61.80; H, 4.75; N, 6.00. Found: C, 61.82; H, 4.67; N, 5.95.

2,3,6-Trihydroxyquinoline (XI, R = OH).—Crude 2,3-dihydroxy-6-methoxyquinoline (0.5 g., 0.0026 mole) was refluxed with a mixture of 48% hydrobromic acid (4 ml.) and glacial acetic acid (4 ml.) for three hours. The reddish-brown solution was diluted with water (150 ml.) and refrigerated for three days. The tan crystals which separated were filtered and recrystallized from hot water using charcoal to give small, cream-colored needles (105 mg., 23%), m.p. 305–315°.

For analysis, the product was recrystallized twice from 30% aqueous methanol using charcoal each time, m.p. 318–319° dec.

Anal. Calcd. for $C_9H_7O_3N$: C, 61.01; H, 3.99; N, 7.91. Found: C, 60.67; H, 4.13; N, 8.14.

A mixed melting point with 2,3,6-trihydroxyquinoline prepared from 4-acetoxyhydrazobenzene showed no depression. Both specimens of 2,3,6-trihydroxyquinoline had identical infrared spectra (Nujol mull).

The acetyl derivative, prepared in the usual manner, melted at 228–229° and did not depress the m.p. of the acetyl derivative of 2,3,6-trihydroxyquinoline prepared from 4-acetoxyhydrazobenzene.

Anal. Calcd. for $C_{11}H_9O_4N$: N, 6.39. Found: N, 6.28.

2,3-Dihydroxyquinoline (VII, R = H). 2-(N-Chloracetamino)-benzaldehyde (X, R = H).—To a solution of 2-aminobenzaldehyde[13] (1.50 g., 0.0124 mole) in anhydrous ether (100 ml.) was added dropwise chloroacetic anhydride (2.5 g., 0.0146 mole) in anhydrous ether (75 ml.) and the reaction mixture allowed to stand at room temperature overnight. After removal of the solvent under reduced pressure, the resulting solid was recrystallized from 80% methanol to give 1.9 g. (78% of theory) of colorless needles, m.p. 105–106°.

Anal. Calcd. for $C_9H_8O_2NCl$: C, 54.70; H, 4.08; N, 7.09; Cl, 17.94. Found: C, 54.58; H, 4.25; N, 7.20; Cl, 17.94.

2,3-Dihydroxyquinoline (XI, R = H).—To a boiling solution of 2-(N-chloracetamino)-benzaldehyde (0.80 g., 4.05 mmoles) in methanol (20 ml.) and water (50 ml.) was added a solution of potassium hydroxide (1.0 g.) in 10 ml. of water in one portion. After refluxing for one hour, the methanol was distilled, the solution treated with charcoal and filtered. On acidification of the filtrate with concentrated hydrochloric acid, a white solid separated which after filtering and washing with 10 ml. of cold water weighed 0.60 g. (92%). The product was recrystallized successively from aqueous 10% methanol (190 ml.), methanol and finally water, using charcoal each time to give small, snow-white needles, m.p. 256–257° uncor. (recorded[3] m.p. 258°). A mixed m.p. with 2,3-dihydroxyquinoline prepared through hydrazobenzene[3] showed no depression. The infrared spectra (Nujol mull) of both samples were identical.

The acetyl derivative made in the usual way melted at 211–212° (recorded[3] m.p. 214°) and did not depress the melting point of the acetyl derivative of 2,3-dihydroxyquinoline made by Diels and Reese[3] *via* hydrazobenzene.

(13) E. Bamberger and E. Demuth, *Ber.*, **34**, 1329 (1901).

CAMAS, WASHINGTON

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

Free Radical Substitution in 3,4-Benzpyrene[1]

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RECEIVED NOVEMBER 10, 1955

Irradiation of 3,4-benzpyrene and thioglycolic acid with a mercury arc in quartz vessels gives a 43% yield of 5-benzpyrenylacetic acid, whose structure is proved by decarboxylation to 5-methylbenzpyrene. 5-Mercaptobenzpyrene appears to be formed also. 5-Benzpyrenylmercaptoacetic acid has been synthesized, and irradiation of its methyl ester decomposes it to yield some methyl 5-benzpyrenylacetate. Azoisobutyronitrile and benzpyrene yield a small amount of a monocyanopropyl product, and an appreciable amount of 1,2-bis-(cyanopropyl)-1,2-dihydrobenzpyrene. The significance of these results for the theoretical calculations of reactivity of benzpyrene is discussed. An improved paper chromatographic technique for benzpyrene and its derivatives is described. Numerous experiments show that benzpyrene is not rapidly attacked by RS radicals.

The study of the action of free radicals on aromatic nuclei is of considerable theoretical and practical interest. The impetus for the present study on free radical attack on the carcinogenic hydrocarbon 3,4-benzpyrene arose during an investigation[2] of the nature of the chemical combination between benzpyrene and skin protein.[3] A possible route for attachment of benzpyrene to cell constituents would involve a free radical attack on the hydrocarbon by a grouping present in tissue.[4] We have therefore investigated a number of systems expected to lead to free radical formation in the presence of benzpyrene, particularly systems in which sulfur radicals, RS·, would be formed.

Irradiation of hydrogen sulfide or a mercaptan by a mercury arc is known to yield RS radicals,[5] which can add to carbon–carbon double bonds. We have found, however, that irradiation of thioglycolic acid and benzpyrene (I) by a mercury arc in a

(1) This research was supported in part by the United States Air Force, through the Office of Scientific Research of the Air Research and Development Command, and in part by the Damon Runyon Memorial Fund for Cancer Research.

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(3) *Cf.* E. C. Miller, *ibid.*, **11**, 100 (1951).

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(5) W. E. Vaughan and F. F. Rust, *J. Org. Chem.*, **7**, 472 (1942); J. I. Cunneen, *J. Chem. Soc.*, 36 (1947).