ported for neoprotoveratrine,[4] yielded *p*-phenylphenacyl acetate, m.p. 110–111°, *p*-phenylphenacyl α-methylbutyrate, m.p. 69–70°, and α-methyl-α,β-dihydroxybutyric acid, m.p. 97–98.5°. The above compounds were further identified by mixed melting points with authentic samples and by their infrared spectra.

Conversion of Neoprotoveratrine to Desacetylneoprotoveratrine by Methanolysis.—Neoprotoveratrine (0.78 g.) was allowed to stand for 15 hours in methanol (100 ml.). At the end of this time, the methanol was evaporated to dryness *in vacuo* and the residue was subjected to a 24-plate countercurrent distribution using the same solvent system employed in the isolation of desacetylneoprotoveratrine. The material recovered from tubes 22–24 (0.262 g.) was crystallized from benzene, yielding clusters of needles (0.12 g.), m.p. 182–183.5°, $[\alpha]^{24}D$ −9.6 ± 2 (*c* 0.99 in py.). A mixed melting point with desacetylneoprotoveratrine isolated directly gave no depression. The infrared spectra of the two compounds were identical. For analysis the sample was dried at 120° (2 mm.) to constant weight.

Anal. Calcd. for $C_{39}H_{61}O_{14}N$: C, 61.00; H, 8.01. Found: C, 60.99; H, 8.02.

In a volatile acid determination 16.31 mg. required 3.654 ml. of 0.01 *N* $Na_2S_2O_3$ or 1.72 equivalents.

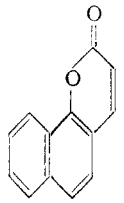
RIKER LABORATORIES, INC.
LOS ANGELES, CALIFORNIA

Preparation of 7,8-Benzocoumarin and 1-Methoxynaphthalene-2-propionic Acid[1]

BY C. F. KOELSCH AND P. T. MASLEY

RECEIVED APRIL 2, 1953

α-Naphthol reacts with malic acid in presence of sulfuric acid to form 7,8-benzocoumarin (I)[2] but



I

the best yields so far reported[3] were only 25–30%. Through systematic experiments it has now been found that nearly double the previous yield can be obtained by using acetic acid as a diluent for the reaction mixture and by using an excess of malic acid.

Experimental

A well ground mixture of 170 g. of technical α-naphthol and 226 g. of technical malic acid was added in portions during 20 minutes to a hot solution of 360 ml. of concd. sulfuric acid in 240 ml. of acetic acid. Gas evolution and some refluxing took place. During the addition and for 90 minutes afterwards, the mixture was stirred and kept at 135–141°. The solution was then stirred into one liter of crushed ice. The resulting mixture was boiled and then cooled while it was being stirred. The crude tarry product was separated, suspended in one liter of boiling water, and treated with enough sodium carbonate to cause the aqueous liquor to turn from dark brown to a reddish color. The mixture was cooled, and the solid was removed and washed with water. The product could be crystallized from acetic acid at this point, but it was usually easier to obtain a colorless product if it was distilled first, b.p. 235–240° at 6 mm., m.p. 141–142°, yield 110–127 g., 45–55%.

Anal. Calcd. for $C_{13}H_8O_2$: C, 79.6; H, 4.1. Found: C, 79.9; H, 4.1.

Reduction of 35 g. of the coumarin dissolved in 200 ml. of 10% sodium hydroxide by treatment with 360 g. of 3% sodium amalgam gave a little dimeric product and mainly **3,4-dihydro-7,8-benzocoumarin**. The product was precipitated with hydrochloric acid, distilled (b.p. 210–220° at 15 mm.) and then crystallized from alcohol, yielding 29 g. of needles, m.p. 76–77°.

Anal. Calcd. for $C_{13}H_{10}O_2$: C, 78.7; H, 5.6. Found: C, 78.7; H, 5.1.

The dihydrocoumarin reacted rapidly with phenylhydrazine in alcohol, forming 1-**hydroxynaphthalene-2-propiophenylhydrazide**, colorless crystals from alcohol, m.p. 176–178° dec.

Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.5; H, 5.9. Found: C, 74.9, 74.2; H, 5.7, 5.9.

The dihydrocoumarin (40 g.) was methylated with aqueous sodium hydroxide and methyl sulfate, giving 80–90% of 1-**methoxynaphthalene-2-propionic acid**, colorless needles from ligroin containing 5% of chloroform, m.p. 94–96°, b.p. *ca.* 240° at 20 mm.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.1; H, 6.1. Found: C, 72.8, 73.2; H, 6.1, 5.7.

1-**Methoxynaphthalene-2-propionamide**, colorless needles from dilute alcohol, m.p. 103–105°, was obtained from the acid with thionyl chloride and ammonium hydroxide.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.3; H, 6.0. Found: C, 73.5; H, 6.3.

SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA
MINNEAPOLIS 14, MINNESOTA

(1) From the M.S. Thesis of Paul Thomas Masley, July, 1942.
(2) V. Pechmann, *Ber.*, **17**, 1651 (1884).
(3) K. Bartsch, *ibid.*, **36**, 1966 (1903).

Direct Halogenation of Some Aromatic Amines

BY GENNADY M. KOSOLAPOFF

RECEIVED MARCH 18, 1953

The complexes between dioxane and halogens which were noted by Favorskii some years ago[1] afford an interesting method for mild direct halogenation of sensitive aromatic compounds. We have examined the bromination of several amines by means of the dioxane–bromine complex and found that monohalogenation can be carried out with moderately good yields without resorting to the customary blocking procedure.

Experimental Part

The complex, an orange-yellow solid, m.p. 64°, is readily prepared in quantity by mixing equimolar amounts of the components and quenching the hot product in ice-water. However, if the material is to be used in solution, it is merely necessary to add the desired amount of bromine to a cooled and stirred mass of dioxane. The bromination of amines can be carried out either by direct addition of the finely powdered complex to a solution of the amine, preferably in dioxane, or by addition of a dioxane solution of the complex to a cooled and stirred solution of the amine in dioxane in the presence of the requisite amount of concentration aqueous alkali. The latter procedure appears to be more economical of the amine.

Aniline.—The complex (25 g.) was added over 15 minutes in its original crystalline state (crystals 1–2 mm. diameter) to 9.3 g. of aniline in 20 g. of dioxane at 5–10° with stirring, in a beaker. The resulting precipitate was filtered off, washed with a little water and dilute sodium hydroxide, and again with water. The product (7 g.) was then dissolved in 75 ml. of hot ethanol and cooled, yielding 1.75 g. of 2,4,6-tribromoaniline. The solution was diluted with two volumes of water and on cooling yielded 4.5 g. (26%) of *p*-bromoaniline, m.p. 66.0–66.5°, characterized by mixed melting point with an authentic specimen and further by conversion to the acetyl derivative, which melted at 165°.

When the above experiment was repeated with finely ground complex which permitted more rapid solution and better distribution of the halogenating agent in the mixture, yields up to 50–57% were obtained and the amount of tribromoaniline declined to a small fraction of a gram.

(1) A. E. Favorskii, *J. Russ. Phys. Chem. Soc.*, **38**, 741 (1906).

Finally, a solution of 16 g. of bromine in 160 ml. of dioxane was added dropwise with good agitation (stirrer near the bottom of the flask) at 5° to a solution of 9.3 g. of aniline in 30 ml. of dioxane and 5.6 g. of potassium hydroxide in 20 ml. of water. The addition was made over two hours. The organic layer was washed with 15 ml. of 40% potassium hydroxide and distilled under reduced pressure to remove the solvent. The residue was recrystallized from dilute alcohol, yielding 68% of *p*-bromoaniline. This was the highest yield attained.

Dimethylaniline.—When 12.1 g. of dimethylaniline was brominated with 16 g. of bromine according to the technique outlined above (*cf.* aniline), there was obtained 80–85% *p*-bromodimethylaniline, m.p. 55°.

***p*-Nitroaniline.**—When 13.8 g. of *p*-nitroaniline was brominated with 16 g. of bromine according to the above technique, there was obtained, after three crystallizations from ethanol, 40–45% yield of 2-bromo-4-nitroaniline, m.p. 104°.

***p*-Toluidine.**—Reaction of 21.4 g. of *p*-toluidine with 32 g. of bromine, under the conditions described above (350 ml. of dioxane total volume; 11.2 g. of potassium hydroxide in 50 ml. of water; temperature, 5–8°) yielded, upon vacuum distillation of the washed reaction product, a fraction, b.p. 142–145° at 22 mm., weighing 22 g., which after crystallization from dilute alcohol gave 19.8 g. of 2-bromo-4-methylaniline, m.p. 25–26°, which yielded the acetyl derivative, m.p. 117–118°; the yield 53%.

Direct bromination of *p*-toluidine with the powdered complex, as described under aniline, gave considerable amounts of the 2,6-dibromo derivative, which melted at 78–79°, and very small amounts of isolated monobromo compound were obtained. This result is expected owing to the high order of aromatic reactivity of this amine.

ROSS CHEMICAL LABORATORY
ALABAMA POLYTECHNIC INSTITUTE
AUBURN, ALABAMA

8-Nitro-7-methoxyisoquinoline

BY MARSHALL KULKA

RECEIVED MARCH 18, 1953

In harmony with theoretical considerations 7-methoxyisoquinoline[1] undergoes nitration in the 8-position. The nitration product, which was obtained in 80% yield, was reduced and the resulting 7-methoxy-8-aminoisoquinoline converted to 7-methoxy-8-chloroisoquinoline. The identity of this was established by comparing with an authentic sample prepared by methylating 7-hydroxy-8-chloroisoquinoline. The latter compound[2] was previously obtained from 2-chloro-3-hydroxybenzaldehyde and aminoacetal.

Experimental

7-Methoxy-8-nitroisoquinoline.—To a stirred solution of 7-methoxyisoquinoline[1] (7.0 g.) in concentrated sulfuric acid (100 cc.) was added portionwise a solution of potassium nitrate (5.0 g.) in concentrated sulfuric acid (35 cc.) while the temperature was maintained at 0–5° by cooling. After stirring for an additional one-half hour at 0–5°, the reaction mixture was poured onto cracked ice. The resulting solution was basified and the yellow precipitate filtered, washed and dried. Crystallization from benzene yielded 7.0 g. (80%) of yellow prisms melting at 164–165°. *Anal.* Calcd. for $C_{10}H_8N_2O_3$: C, 58.83; H, 3.92; N, 13.73. Found: C, 58.66, 58.70; H, 3.97, 3.64; N, 13.53.

7-Methoxy-8-aminoisoquinoline.—To a stirred solution of 7-methoxy-8-nitroisoquinoline (6.0 g.) in concentrated hydrochloric acid (30 cc.) was added portionwise a solution of stannous chloride dihydrate (30 g.) in concentrated hydrochloric acid (50 cc.) while the temperature was maintained at 35–40° by cooling. Then the reaction mixture was allowed to stand at room temperature overnight with occasional cooling during the first hour in order to keep the temperature below 40°. The reaction mixture was diluted with an equal volume of water and then added to a mixture of 30% sodium hydroxide solution (300 cc.) and cracked ice (about 300 g.). The precipitated amine was extracted with three 400-cc. portions of ether and the ether was removed from the extract. Crystallization of the residue from benzene yielded 3.8 g. (74%) of yellow needles melting at 156–157°. *Anal.* Calcd. for $C_{10}H_{10}N_2O$: C, 68.97; H, 5.75; N, 16.10. Found: C, 69.12, 69.25; H, 5.83, 5.99; N, 15.90.

7-Methoxy-8-chloroisoquinoline.—A solution of 7-methoxy-8-aminoisoquinoline (0.6 g.) in concentrated hydrochloric acid (2 cc.) and water (10 cc.) was diazotized at 0° with sodium nitrite (0.25 g.) in water (5 cc.). The resulting diazonium chloride solution was added to a solution of cuprous chloride (2 g.) in concentrated hydrochloric acid (20 cc.) previously warmed to 70°. After standing overnight the reaction mixture was basified and steam distilled. The steam distillate was filtered and the white solid (0.32 g. or 50%) was crystallized from methanol, white needles, m.p. 124–125°. The methylation of 7-hydroxy-8-chloroisoquinoline[2] with diazomethane yielded a compound melting at 124–125° alone or in admixture with the compound above. *Anal.* Calcd. for $C_{10}H_8NOCl$: C, 62.02; H, 4.14; N, 7.23. Found: C, 62.43, 62.44; H, 4.26, 4.37; N, 7.20.

DOMINION RUBBER COMPANY, LIMITED
RESEARCH LABORATORY
GUELPH, ONTARIO

(1) von P. Fritsch, *Ann.*, **286**, 1 (1895).

(2) R. H. F. Manske and M. Kulka, *Can. J. Research*, **B27**, 161 (1949).

Quinoxaline Studies. V. Synthesis of 2-Hydroxy-3,5-dimethylquinoxaline and 2-Hydroxy-3,8-dimethylquinoxaline

BY GEORGE KYRYACOS[1] AND HARRY P. SCHULTZ

RECEIVED SEPTEMBER 3, 1952

Although a number of papers have discussed the synthesis of unsymmetrically substituted quinoxalines with substituents in the 6- and 7-position of the quinoxaline ring, no work has been reported with substituents in the 5- and 8-positions of the unsymmetrically substituted quinoxaline ring. The purpose of this investigation was to synthesize and determine the physical properties of 2-hydroxy-3,5-dimethylquinoxaline and 2-hydroxy-3,8-dimethylquinoxaline.

The starting material for the synthesis of 2-hydroxy-3,5-dimethylquinoxaline was 2-amino-3-nitrotoluene. *o*-Acetotoluidide was nitrated by the procedure used by Bacharach[2] to nitrate *p*-acetotoluidide. Hydrolysis of the 3-nitro-2-acetotoluidide, followed by steam distillation, gave 2-amino-3-nitrotoluene. Condensation of 2-amino-3-nitrotoluene with α-bromopropionic acid gave N-(2-nitro-6-methylphenyl)-*dl*-α-alanine.

The amino acid, N-(2-nitro-6-methylphenyl)-*dl*-α-alanine, was reduced catalytically to the dihydro derivative of 2-hydroxy-3,5-dimethylquinoxaline. The unisolated 3,4-dihydro-2-hydroxy-3,5-dimethylquinoxaline was oxidized by basic hydrogen peroxide solution to 2-hydroxy-3,5-dimethylquinoxaline.

The preparation of 2-hydroxy-3,8-dimethylquinoxaline utilized similar reactions, starting with 2-nitro-3-aminotoluene, which was prepared by the procedure of Hoogewerff and van Dorp.[3] Higher yields of substituted alanine derivative were ob-

(1) Abstracted from the M.S. thesis of George Kyryacos, The University of Miami, 1952.

(2) C. Bacharach, THIS JOURNAL, **49**, 1522 (1927).

(3) S. Hoogewerff and W. van Dorp, *Rec. trav. chim.*, **8**, 1921 (1889).