Anal. Calcd. for $C_{26}H_{39}O_2N$: N, 3.52. Found: N, 3.82.

It was 95.5% pure as a secondary amine apparently still containing traces of diisopropyl-*p*-anisidine. The hydrochloride was prepared by dissolving the compound in ether and adding 36% hydrochloric acid.

Anal. Calcd. for $C_{26}H_{38}O_2N{\cdot}HCl$: N, 3.23; Cl, 8.18. Found: N, 3.63; Cl, 8.9.

p-Anisidine and Cyclohexanol.—*p*-Anisidine (95.5 g., 0.77 *M*), cyclohexanol (200 g., 2 *M*), H_2F_2 (386 g.), 10–20° thirty minutes, 20° eighteen hours. An oil separated when the condensation mass was poured onto water. It was dissolved in benzene, washed with water, clarified by filtration and concentrated to a small volume. Petroleum ether was then added to precipitate the product in a crystalline form. Monocyclohexyl-*p*-anisidine tetrahydrofluoride (50 g., 22.8%, m. p. 185–195°) was obtained. It was of interest that this hydrofluoride was soluble in benzene.

Anal. Calcd. for $C_{13}H_{19}ON{\cdot}H_4F_4$: N, 4.91. Found: N, 4.83.

The hydrofluoride was based and converted to the hydrochloride which melted from 225–230°.

Anal. Calcd. for $C_{13}H_{19}ON{\cdot}HCl$: N, 5.80; Cl, 14.7. Found: N, 5.75; Cl, 14.46. By nitrite absorption: 99% pure.

1-Diethylamino-3-ethoxybenzene and Isopropyl Ether.—N-Diethyl-*m*-phenetole (88 g., 0.45 *M*), isopropyl ether (51 g., 0.5 *M*), H_2F_2 (303 g.), 10–20° thirty minutes, 20° twenty hours. The finished reaction mass was poured onto an excess of aqueous ammonia and the product which separated was dissolved in benzene. Monoisopropyl-1-diethylamino-3-ethoxybenzene (84 g., 79.5%) distilled at 110° at 0.15 mm. as a dark colored oil which was only sparingly soluble in aqueous hydrochloric acid.

Anal. Calcd. for $C_{15}H_{25}ON$: N, 5.95. Found: 5.99.

1-Amino-2-methoxynaphthalene and Isopropyl Ether.—1-Amino-2-methoxynaphthalene (104 g., 0.6 *M*), isopropyl ether (102 g., 1 *M*), H_2F_2 (435 g.), 5–10° one hour, 20° twenty hours. The condensation product separated as an oil when poured onto water. Triisopropyl-1-amino-2-methoxynaphthalene (83 g., 46.3%, b. p. 169° at 0.14 mm.) was obtained as a viscous oil which was only sparingly soluble in aqueous hydrochloric acid, but diazotized and coupled.

Anal. Calcd. for $C_{20}H_{29}ON$: N, 4.68. Found: N, 4.52.

Summary

It has been shown that hydrofluoric acid is an effective acid condensing agent for the preparation of nuclear alkylated isocyclic compounds.

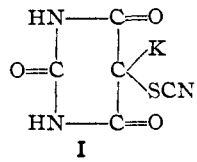
WILMINGTON, DEL. RECEIVED OCTOBER 27, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF MISSOURI]

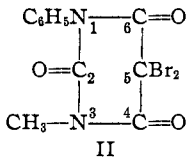
Phenyl Alkyl Nitrogen Substitution and Reactivity in the Barbituric Acid Series

BY DOROTHY NIGHTINGALE AND R. G. TAYLOR[1]

5,5-Dibromobarbituric acid reacts vigorously with ammonia to form an ammonium salt of 5-bromobarbituric acid,[2] with thiourea to form thiopseudo uric acid and with potassium thiocyanate to form (I)[3]



I



II

In this Laboratory, Morris[4] found that 1-phenyl-5,5-dibromobarbituric acid reacted with these same reagents but much less vigorously, to form the same derivatives. The amine salts of 1-phenyl-5-bromobarbituric acid were unstable as compared with the corresponding salts of 5-bromobarbituric acid. The 1,3-diphenyl-5,5-dibromobarbituric acid either did not react at all under the same conditions or formed some tarry material which would not yield crystals.

The progressive differences in reactivity of the halogen atoms as one or both of the hydrogens attached to nitrogen were replaced by phenyl groups led to the questions: is it the fact that the substituting groups on the nitrogens are aryl, which affects the reactivity, or would alkyl groups have the same effect?

To answer these questions, 5,5-dibromo-1-phenyl-3-methylbarbituric acid (II) and 5,5-dibromo-1-phenyl-3-butyl-barbituric acid (III) have been prepared and their reactions studied with amines, thiourea, and potassium thiocyanate.

Their behavior paralleled that of the corresponding diaryl nitrogen substituted barbituric acids. Replacement of an aryl group by an alkyl group increased the solubility of the acids in organic solvents and lowered the melting points.

Hepner and Frenkenberg[5] describe the prepa-

(1) Abstract of a dissertation presented by Richard G. Taylor in partial fulfilment of the requirements for the degree of Master of Arts at the University of Missouri.

(2) Biltz and Hamburger, *Ber.*, **49**, 635 (1916).

(3) Trzcinski, *ibid.*, **16**, 1057 (1883).

(4) Nightingale and Morris, THIS JOURNAL, **58**, 1469 (1936).

(5) Hepner and Frenkenberg, *J. prakt. Chem.*, **134**, 249 (1932).

ration of 5-bromo-1-phenyl-3-methylbarbituric acid from the acid and bromine in chloroform solution. The compound was reported as having a melting point of 161° and on analysis gave 26.93% bromine. Their procedure was used many times and always gave a product which melted at 161°, but it contained 42.52% bromine, proving the compound to be the 5,5-dibromo acid.

The preparation of the mono nitrogen substituted barbituric acids either from a mono R-urea and malonyl chloride, or from the urea, malonic acid and phosphorus oxychloride, has given small yields of a product often difficult to purify.[6] By modifying the procedure of Hepner and Frenkenberg,[5] these monosubstituted barbituric acids were obtained readily in good yield.

Experimental

Phenyl methyl urea and phenyl *n*-butyl urea were prepared according to the procedure of Scholl and Holdermann.[7] For the preparation of phenyl *n*-butyl urea, not described in the literature, 119 g. of phenyl isocyanate was dissolved in 1500 cc. of anhydrous ether. The well-dried *n*-butylamine (73 g.) was added slowly to the ether solution, with stirring. The urea precipitated as rapidly as it was formed, in quantitative yield. It crystallized from hot water in white needles which melted at 135°.

Anal. Calcd. for $C_{11}H_{16}ON_2$: N, 14.58. Found: (Kjeldahl) N, 14.62.

The 1-phenyl-3-methylbarbituric acid was prepared by the following modification of the procedure of Hepner and Frenkenberg:[5] molar quantities of phenylmethylurea (150 g.) and malonic acid (104 g.) were mixed with 2.4 moles (245 g.) of acetic anhydride and heated slowly until all the urea and malonic acid had dissolved. The flask was placed on a water-bath, evacuated to 18–20 mm., and warmed so that most of the acetic anhydride distilled slowly. The residue was treated with 0.2 *N* sodium hydroxide to dissolve the barbituric acid, and the unchanged urea removed by filtration. The clear solution was acidified with 0.2 *N* hydrochloric acid to precipitate the 1-phenyl-3-methylbarbituric acid. The average yield was about 80%.

The 1-phenyl-3-*n*-butylbarbituric acid was prepared by the same procedure. The product, recrystallized from alcohol in colorless needles, melted at 96–98°. The yield was 65%.

Anal. Calcd. for $C_{14}H_{16}O_3N_2$: N, 10.77. Found: N, 10.79.

1-*o*-Tolylbarbituric acid, m. p. 181°, was prepared similarly from 15 g. of *o*-tolyl urea and 10 g. of malonic acid dissolved in 50 g. of acetic anhydride. This urea is not readily soluble in acetic anhydride and therefore required twice as much of the anhydride as for the other barbituric acids. The yield was 50%, as compared with 10% using the malonyl chloride procedure.

Anal. Calcd. for $C_{11}H_{10}O_3N_2$: N, 12.84. Found: N, 12.95.

Other monosubstituted ureas gave equally good yields of the corresponding 1-R-barbituric acid.

The 5-anilinomethylene derivatives of these barbituric acids were prepared according to the procedure previously described.[6a]

Barbituric acid	Formula	M. p., °C.	% Nitrogen Calcd.	Found
1-Phenyl-3-methyl	$C_{18}H_{15}O_3N_3$	170	13.07	12.97
1-Phenyl-3-butyl	$C_{21}H_{21}O_3N_3$	146–148	11.57	11.67

The 5,5-dibromo-1-phenyl-3-methylbarbituric acid was prepared as follows. The theoretical amount of bromine (22.5 g.) was dissolved in glacial acetic acid (60 cc.) and added slowly with constant stirring to a solution of 15 g. of the barbituric acid in 150 cc. of acetic acid. After the mixture had been stirred for forty-five minutes it was poured over cracked ice. The precipitated dibromo acid was collected on a Büchner funnel, washed thoroughly with water and recrystallized from alcohol. An almost quantitative yield of slightly colored crystals was obtained, m. p. 161°.

Anal. Calcd. for $C_{11}H_8O_3N_2Br_2$: C, 35.11; H, 2.14; N, 7.45; Br, 42.52. Found: C, 35.34; H, 2.37; Br, 42.65; N, 7.52.

Glacial acetic acid was found to be the most convenient solvent for bromination of the nitrogen substituted barbituric acids.

The 5,5-dibromo-1-phenyl-3-*n*-butylbarbituric acid was prepared in the same way from 16.7 g. of bromine in 40 cc. of glacial acetic acid, and 10 g. of the barbituric acid dissolved in 100 cc. of acetic acid. The yield was 70%. The crystals, almost white, melted at 108–110°.

Anal. Calcd. for $C_{14}H_{14}O_3N_2Br_2$: Br, 38.24; N, 6.70. Found: Br, 38.26; N, 6.83.

The 5,5-dibromo-1,3-di-*o*-tolylbarbituric acid was prepared from 10.4 g. of bromine in 30 cc. of acetic acid and 10 g. of the barbituric acid in 100 cc. of glacial acetic acid. The yield was quantitative. The crystals melted at 190–191°.

Anal. Calcd. for $C_{18}H_{14}O_3N_2Br_2$: Br, 34.28; N, 6.01. Found: Br, 34.19; N, 5.91.

The 5,5-Dibromo N-Substituted Barbituric Acids with Thiourea, Potassium Thiocyanate, and Amines.—Refluxing a solution of either (II) or (III) with thiourea in alcohol solution for eight hours gave no visible evidence of a reaction. The alcohol was evaporated and the residue extracted carefully. About 50% of the thiourea was recovered, but no product corresponding to a thiopseudo uric acid could be obtained.

Potassium thiocyanate failed to react with either (II) or (III).

Amines gave only a tarry product even at low temperatures and using benzene as a solvent.

Summary

The substitution of one methyl or one butyl group in place of a phenyl group in 1,3-diphenyl-5,5-dibromobarbituric acid does not appear to

(6) (a) Nightingale and Alexander, THIS JOURNAL, **58**, 794 (1936); (b) Kashkin, *J. Gen. Chem.* (*U. S. S. R.*), **5**, 1460 (1935); *C. A.*, **30**, 2177 (1936).

(7) Scholl and Holdermann, *Ann.*, **345**, 382 (1906).

promote a reaction of the halogens with such reagents as thiourea, potassium thiocyanate, or amines.

The 1-phenyl-3-methyl- and 3-*n*-butylbarbituric acids, their 5,5-dibromo, and their 5-anilinomethylene derivatives have been prepared.

A convenient procedure has been developed which gives satisfactory yields of both mono and di nitrogen substituted barbituric acids from the substituted urea and malonic acid in acetic anhydride solution.

COLUMBIA, MO. RECEIVED JANUARY 26, 1939

[CONTRIBUTION NO. 159 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

The Nitrogen Compounds in Petroleum Distillates. XIV. Isolation of 2,4-Dimethyl-8-ethylquinoline from the Kerosene Distillate of California Petroleum[1]

BY W. NELSON AXE[2]

Introduction

The positions of alkylation of kero quinolines thus far isolated in the Texas Laboratory are 2, 3, 4 and 8 with a methyl invariably at position 2. Substitution at positions 5, 6 or 7 has not been observed, whereas we now have examples of two bases with an ethyl at 8 and two with an *n*-propyl at 8. In this paper is reported the discovery of 2,4-dimethyl-8-ethylquinoline, along with proof of its structure through degradation and synthesis.

Since completion of the research reported in this paper, another base of the composition, $C_{14}H_{17}N$[3] has been identified through degradation and synthesis as 2,4-dimethyl-8-*n*-propylquinoline.

It is of interest to note that alkylation higher than methyl has not been encountered in the pyridine nucleus of any of the following ten kero quinolines isolated in the Texas Laboratory: 2,3-,[4] 2,4-[4] and 2,8-dimethylquinoline[5]; 2,3,8-[6], and 2,4,8-trimethylquinoline[7]; 2,3,4,8-tetramethylquinoline[3]; 2,3-dimethyl-8-ethyl-[8] and 2,4-dimethyl-8-ethylquinoline; 2,3-dimethyl-8-*n*-propylquinoline[3] and 2,4-dimethyl-8-*n*-propylquinoline.

Kero quinoline homologs alkylated at positions 2, 3 and 8 occur in relatively large quantities, whereas homologs alkylated at positions 2, 4 and 8 have been encountered only in small amounts; as an example, only 4 g. of 2,4-dimethyl-8-ethylquinoline was available for characterization and proof of structure.

Experimental

The crude kero bases, as received from the Union Oil Company, were refined through the following procedures: I, fractional acid extraction; II, fractional distillation under atmospheric and under reduced pressure; III, cumulative extraction.[7]

At the end of each step recombinations of fractions in the order of boiling points and refractive indices were made and the new fractions were employed in the next step.

Since the objective in this investigation was the isolation and identification of *aromatic* bases associated with 2,3-dimethyl-8-ethylquinoline (b. p. 284.6°), the *non-aromatics*, which in step III were segregated as hydrochlorides in the *chloroform* layer, were not investigated.

Isolation of 2,4-Dimethyl-8-ethylquinoline.—The separate fractions of *aromatic* bases present in step III as hydrochlorides in the *aqueous* layer were liberated and, after exhaustive distillation, cuts within the boiling range of 290–291° were combined and processed for 2,3-dimethyl-8-ethylquinoline previously isolated by Key and Bailey.[8] This base is conveniently removed as the acid sulfate by the addition of concd. sulfuric acid to an alcohol–acetone solution of the base mixture. The yield from the purified acid sulfate amounted to 18.5% of the original aromatic fraction.

The residual bases from the above 290–291° fraction (460 cc., d^{20}_4 1.0074, $n^{20}D$ 1.5846) were processed through counter-current extraction using Schutze's[9] modification of the Jantzen[10] column.

The 460 cc. of the bases was mixed with petroleum ether to a volume of 1380 cc.; 2 *N* hydrochloric acid in an amount sufficient to neutralize 330 cc. of the bases (calculation based on mol. wt., 185) was diluted likewise to 1380 cc. The acid was fed in at the top of the column at the same rate as the base solution entered the bottom, intimate contact of the acid and bases being attained with a

(1) Acknowledgment is due Professor J. R. Bailey for the cooperation extended in supplying the fractions of bases used in this work. The original crude bases were furnished by the Union Oil Company of California.

(2) Research Department, Phillips Petroleum Company, Bartlesville, Okla.

(3) Axe and Bailey, THIS JOURNAL, **60**, 3028 (1938).

(4) Biggs and Bailey, *ibid.*, **55**, 4141 (1933).

(5) Lake and Bailey, *ibid.*, **55**, 4143 (1933).

(6) King and Bailey, *ibid.*, **52**, 1239 (1930).

(7) Perrin and Bailey, *ibid.*, **55**, 4136 (1933).

(8) Key and Bailey, *ibid.*, **60**, 763 (1938).

(9) Schutze, Quebedeaux and Lochte, *Ind. Eng. Chem., Anal. Ed.*, **10**, 675 (1938).

(10) Jantzen, "Das fraktionierte Destillieren und das fraktionierte Verteilen," Verlag Chemie, Berlin, 1932, pp. 108–116.