

[CONTRIBUTION FROM THE LABORATORIES OF GEORGE A. BREON &amp; CO., STERLING DRUG CO., INC.]

**Analgesics. III. Hydrochlorides of Phenylalkylamines<sup>1</sup>**BY L. H. GOODSON<sup>2</sup> AND R. B. MOFFETT<sup>3</sup>

As reported in the two earlier papers in this series,<sup>4,5</sup> our laboratory is interested in the synthesis of analgesic agents selected from the group of compounds known as the phenylalkylamines. The present paper is a continuation of our earlier work and describes thirty-one additional amines which are listed in Table I.

The synthetic methods used in the preparation of these compounds are not new, but are described briefly in the experimental part. The yields given usually do not indicate the best possible, but, rather, those actually obtained in one preparation.

These compounds have been screened for their analgesic activity by Dr. Harold G. Holck of the University of Nebraska, School of Pharmacy, and publication of results will appear elsewhere. Little or no analgesic activity was exhibited by any of these compounds when compared with morphine or isonipicaine.

**Experimental**

**Amino Ketones and Esters, 1-13 (Table I).**—The starting materials, desoxybenzoin, desoxyanisoin,  $\alpha$ -cyclohexylacetophenone,<sup>6</sup>  $\alpha$ -cyclohexyl-*p*-methoxyacetophenone,<sup>7</sup> 2-naphthyl benzyl ketone<sup>8</sup> and ethyl phenylacetate, were readily available or were prepared by the usual methods. These compounds were brominated by adding the calculated quantity of bromine to a solution of the compound in carbon tetrachloride. The resulting  $\alpha$ -bromo compounds were freed of solvent and then used with or without distillation. Each of the crude bromo compounds in absolute ether or benzene was allowed to react with an excess of the appropriate amine, either by allowing the mixture to stand at room temperature for one week or by refluxing for two hours. The product was separated from the excess of reactants by treating the reaction mixture with aqueous sodium hydroxide, washing the organic layer with water, and evaporating to dryness, finally at 80° *in vacuo*. The base was taken up in absolute ether and the hydrochloride was precipitated by passing in hydrogen chloride.

**Amino Alcohols, 14-17 (Table I).**—These compounds were prepared from the corresponding amino ketones by reduction of the free bases with aluminum isopropoxide in absolute isopropyl alcohol. The slow distillation of the isopropyl alcohol was continued until no trace of acetone was observed in the distillate (eight to fourteen hours). The isopropyl alcohol was then removed under reduced pressure and the residue was shaken with ether and water.

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(4) L. H. Goodson, C. J. W. Wiegand and Janet Splitter, *THIS JOURNAL*, **68**, 2174 (1946).

(5) R. B. Moffett and W. M. Hoehn, *ibid.*, **69**, 1792 (1947).

(6) E. D. Venus-Danilova and A. I. Bol'shukhin, *J. Gen. Chem. (U. S. S. R.)*, **9**, 975-984 (1939); *C. A.*, **33**, 8595 (1939).

(7) P. Ruggli and A. Businger, *Helv. Chim. Acta*, **24**, 1112-1126 (1941); *C. A.*, **36**, 2547 (1942).

(8) J. W. Cook and C. L. Hewett, *J. Chem. Soc.*, 365-377 (1934); P. Ruggli and M. Reinert, *Helv. Chim. Acta*, **9**, 67-79 (1926).

The ether layer was dried over potassium carbonate, and dry hydrogen chloride was passed in.

**Amino Alcohols, 18-19 (Table I).**—These compounds were prepared by the method of Erlenmeyer,<sup>9</sup> in which benzaldehyde is condensed with glycine in the presence of alcoholic alkali to give iso-1,2-diphenylethanolamine. In the present reactions, 2,3-dimethoxybenzaldehyde and 3,4-dimethoxybenzaldehyde were used in place of benzaldehyde. By analogy with the literature we have designated these DL-pairs as *iso* compounds, although we have no evidence concerning the spatial relationships; the so-called normal forms are not yet described.

**Amino Alcohol, 20, and Amine, 27 (Table I).**—The benzene solution of anisoin or desoxyanisoin was mixed with the amine (ethanolamine or benzylamine), a drop of acetic acid added and the mixture refluxed using a continuous water separator until no more water was liberated. The benzene was removed and the resulting crude ketimine was reduced by dissolving it in absolute ethanol and adding five times the theoretical quantity of sodium required to reduce the double bond. The alcohol was removed and the basic organic material was separated, dried, dissolved in absolute ether, and treated with hydrogen chloride.

**Amines, 21-23 (Table I).**—These compounds were prepared from 2-acetonaphthone and dibenzyl ketone by use of the Leuckart reaction.<sup>4</sup> The amines used were  $\beta$ -(4-morpholino)-ethylamine and ethanolamine and during the reaction time of three hours the temperature was raised from 170 to 200°. The formyl derivative was hydrolyzed and the products isolated as described earlier.

**Amines, 24-26 (Table I).**—These compounds were prepared from the corresponding 1,2-di-(*p*-methoxyphenyl)-ethylamines by dissolving them in 48% hydrobromic acid, and boiling them for one-quarter to two hours, then separating the demethylated fraction first by its solubility in alkali and then by recrystallization of the demethylated material after its conversion to its hydrochloride or hydrobromide.

**Amine, 28 (Table I).  $\alpha$ -Phenyl-2-hydroxy-5-cyclohexylacetophenone and Oxime.**—A mixture of 88.1 g. (0.5 mole) of *p*-cyclohexylphenol and 77.3 g. (0.5 mole) of phenylacetyl chloride was warmed on a boiling water-bath until no more hydrogen chloride was evolved (about one and one-half hours). This crude ester was mixed with 84 g. (0.63 mole) of anhydrous aluminum chloride and heated in an oil-bath. At a temperature of 120°, hydrogen chloride was rapidly evolved and at 140° the mixture became very thick. After fifteen minutes at this temperature, it was cooled and decomposed with ice and hydrochloric acid. The product was taken up in ether, washed with water, and after removing the ether, it was distilled first from a Claisen flask and then through a six-inch glass helices-packed column. The fraction, boiling at 120-130° (0.007 mm.), was a light yellow viscous liquid which crystallized on standing. Recrystallization from petroleum ether gave 53.8 g. (37%) of material, m. p. 55-58°.

The oxime was prepared by refluxing for one and one-half hours a solution of 20 g. of the ketone and 20 g. of hydroxylammonium chloride in 50 ml. of ethanol and 50 ml. of pyridine. On evaporation and dilution with water, the oxime crystallized, and a sample was recrystallized from ethanol, m. p. 138.5-140°.

*Anal.* Calcd. for C<sub>20</sub>H<sub>23</sub>NO<sub>2</sub>: N, 4.53. Found: N, 4.64.

**1-(2-Hydroxy-5-cyclohexylphenyl)-2-phenylethylamine (28).**—To a solution of 22.4 g. of the crude oxime in 1 l. of absolute ethanol was added 69 g. of sodium. When

(9) Erlenmeyer, *Ann.*, **307**, 97 (1899); A. Lespagnol, G. Bizard and J. Turlur, *J. Bull. Sci. Pharmacol.*, **43**, 555-571 (1936).

TABLE I

No.	R	R'	$\begin{array}{c} \text{X} \\   \\ \text{R}-\text{C}-\text{CH}-\text{R}' \\    \quad   \\ \text{O} \quad \text{X} \end{array}$	M. p. of HCl deriv., C°. <sup>ff</sup>	Formula	Analyses, %		Ap- prox. yield. %
						Calcd.	Found	
1	Phenyl	Phenyl	Methylamino	216-220 <sup>g</sup>	C <sub>16</sub> H <sub>16</sub> ClNO	Cl, 13.56	13.62	15
2	Phenyl	Phenyl	Diethylamino	184-188 <sup>h</sup>	C <sub>18</sub> H <sub>22</sub> ClNO	Cl, 11.67	11.64	73
3	Phenyl	Phenyl	1-Piperidyl	239-242 <sup>i,j</sup>	C <sub>18</sub> H <sub>22</sub> ClNO	Cl, 11.23	11.24	85 <sup>g</sup>
4	Phenyl	Phenyl	4-Morpholinyl	198-200 <sup>g,dd</sup>	C <sub>18</sub> H <sub>20</sub> ClNO <sub>2</sub>	Cl, 11.16	11.05	20
5	<i>p</i> -Methoxyphenyl	<i>p</i> -Methoxyphenyl	1-Piperidyl	Oil	C <sub>21</sub> H <sub>26</sub> NO <sub>2</sub> <sup>k</sup>	N, 4.14	4.23	59 <sup>g</sup>
6	Phenyl	Cyclohexyl	1-Piperidyl	231-234 <sup>i,ee</sup>	C <sub>18</sub> H <sub>23</sub> ClNO	Cl, 11.02	11.09	56
7	Phenyl	Cyclohexyl	4-Morpholinyl	240-241 <sup>i</sup>	C <sub>18</sub> H <sub>20</sub> ClNO <sub>2</sub>	Cl, 10.95	10.73	69
8	<i>p</i> -Methoxyphenyl	Cyclohexyl	Methylamino	217-219 <sup>g</sup>	C <sub>15</sub> H <sub>24</sub> ClNO <sub>2</sub> <sup>d</sup>	Cl, 11.91	12.14	19
9	<i>p</i> -Methoxyphenyl	Cyclohexyl	1-Piperidyl	220-222.5 <sup>m</sup>	C <sub>20</sub> H <sub>26</sub> ClNO <sub>2</sub> <sup>d</sup>	Cl, 10.07	9.94	20
10	2-Naphthyl	Phenyl	1-Piperidyl	191-193 d. <sup>n</sup>	C <sub>23</sub> H <sub>24</sub> ClNO <sup>b</sup>	Cl, 9.69	9.59	77
11	2-Naphthyl	Phenyl	4-Morpholinyl	216-219 d. <sup>g</sup>	C <sub>22</sub> H <sub>22</sub> ClNO <sub>2</sub> <sup>b</sup>	Cl, 9.64	9.74	66.5
12	Ethoxy	Phenyl	Allylamino	120.5-122 <sup>g,*</sup>	C <sub>17</sub> H <sub>19</sub> ClNO <sub>2</sub> <sup>c</sup>	Cl, 13.92	13.86	77
13	Ethoxy	Phenyl	1-Piperidyl	174-175 d. <sup>p</sup>	C <sub>15</sub> H <sub>22</sub> ClNO <sub>2</sub>	Cl, 12.37	12.46	77
			$\begin{array}{c} \text{R}-\text{CH}-\text{CH}-\text{R}' \\   \quad   \\ \text{OH} \quad \text{X} \end{array}$					
14	Phenyl	Phenyl	1-Piperidyl	240-243 <sup>g,oo</sup>	C <sub>19</sub> H <sub>21</sub> ClNO	Cl, 11.16	11.14	22
15	Phenyl	Cyclohexyl	1-Piperidyl	223-226 d. <sup>i</sup>	C <sub>18</sub> H <sub>20</sub> ClNO	Cl, 10.95	11.02	33
16	Phenyl	Cyclohexyl	4-Morpholinyl	223-224 <sup>g</sup>	C <sub>18</sub> H <sub>20</sub> ClNO <sub>2</sub>	Cl, 10.90	10.91	45
17	<i>p</i> -Methoxyphenyl	Cyclohexyl	1-Piperidyl	205-215 <sup>g</sup>	C <sub>20</sub> H <sub>22</sub> ClNO <sub>2</sub> <sup>d</sup>	Cl, 10.02	9.98	43
18	3,4-Dimethoxyphenyl	3,4-Dimethoxyphenyl	Amino <sup>g</sup>	140-145 <sup>g</sup>	C <sub>13</sub> H <sub>24</sub> ClNO <sub>2</sub> <sup>f</sup>	Cl, 9.59	9.86	4
19	2,3-Dimethoxyphenyl	2,3-Dimethoxyphenyl	Amino <sup>g</sup>	120-121 <sup>g,*</sup>	C <sub>13</sub> H <sub>24</sub> ClNO <sub>2</sub> <sup>f</sup>	Cl, 9.59	9.56	15
20	<i>p</i> -Methoxyphenyl	<i>p</i> -Methoxyphenyl	Benzylamino	195-200 <sup>g</sup>	C <sub>23</sub> H <sub>26</sub> ClNO <sub>2</sub>	Cl, 8.87	8.83	82
			$\begin{array}{c} \text{R}-\text{CH}_2-\text{CH}-\text{R}' \\   \\ \text{X} \end{array}$					
21	Hydrogen	2-Naphthyl	2-(4-Morpholinyl)-ethyl amino	208-210 <sup>g,t</sup>	C <sub>18</sub> H <sub>24</sub> N <sub>2</sub> O <sup>d</sup>	N, 9.85	10.02	70 <sup>g</sup>
22	Hydrogen	2-Naphthyl	2-Hydroxyethylamino	180-182 <sup>g</sup>	C <sub>14</sub> H <sub>16</sub> ClNO <sup>d</sup>	Cl, 14.10	14.00	84 <sup>g</sup>
23	Phenyl	Benzyl	2-Hydroxyethylamino	95-97 <sup>g,*</sup>	C <sub>17</sub> H <sub>22</sub> ClNO <sup>d</sup>	Cl, 12.17	11.97	36 <sup>g</sup>
24	<i>p</i> -Hydroxyphenyl	<i>p</i> -Hydroxyphenyl	Amino	267 d. <sup>u</sup>	C <sub>14</sub> H <sub>14</sub> ClNO <sub>2</sub> <sup>g</sup>	N, 5.27	5.24	25
25	<i>p</i> -Hydroxyphenyl	<i>p</i> -Hydroxyphenyl	Methylamino	170-172 <sup>g</sup>	C <sub>15</sub> H <sub>16</sub> BrNO <sub>2</sub> <sup>g</sup>	Br, 24.64	24.32	50
26	<i>p</i> -Hydroxyphenyl	<i>p</i> -Hydroxyphenyl	Ethylamino	192-195 <sup>g,a,v</sup>	C <sub>15</sub> H <sub>20</sub> BrNO <sub>2</sub> <sup>g</sup>	N, 4.14	4.21	25
27	<i>p</i> -Methoxyphenyl	<i>p</i> -Methoxyphenyl	2-Hydroxyethylamino	126-127 <sup>g</sup>	C <sub>18</sub> H <sub>24</sub> ClNO <sub>2</sub>	Cl, 10.49	10.42	18
28	Phenyl	5-Cyclohexyl-2-hydroxyphenyl	Amino	224-227 <sup>g</sup>	C <sub>20</sub> H <sub>26</sub> ClNO	Cl, 10.68	10.82	40
Miscellaneous amines								
29	N-Methyl- $\alpha$ -cyclohexylbenzylamine			251-253 <sup>g</sup>	C <sub>14</sub> H <sub>22</sub> ClN	Cl, 14.79	14.73	25 <sup>g</sup>
30	1-( <i>p</i> -Chlorophenyl)-1-phenyl-2-aminopropanol			238-243 <sup>g</sup>	C <sub>15</sub> H <sub>17</sub> Cl <sub>2</sub> N <sup>d,bb</sup>	Cl, 11.90	11.70	10
31	1,2-Di- <i>p</i> -methoxyphenylbutylamine			269-271 <sup>w</sup>	C <sub>18</sub> H <sub>24</sub> ClNO <sub>2</sub> <sup>d</sup>	Cl, 11.02	11.05	32

<sup>a</sup> Prepared by R. F. Shrimpton, formerly of this Laboratory. <sup>b</sup> Prepared by Jack Linsk, formerly of this Laboratory. <sup>c</sup> Prepared by Charlotte Hart, formerly of this Laboratory. <sup>d</sup> Prepared by Janet S. Splitter, formerly of this Laboratory. <sup>e</sup> Prepared by C. J. W. Wiegand, formerly of this Laboratory. <sup>f</sup> Prepared by Eugene Klein, formerly of this Laboratory. <sup>g</sup> Crystallized from absolute ethanol. <sup>h</sup> Crystallized from methyl ethyl ketone. The free base distills at 158-165° at 3 mm. <sup>i</sup> Crystallized from ether-alcohol mixture. <sup>j</sup> The free base is reported to melt at 82° by Rabe, *Ber.*, **45**, 2169 (1912); "Beilstein," **20**, 14; R. E. Lutz, J. A. Freek and R. S. Murphey, *THIS JOURNAL*, **70**, 2016 (1948), report the hydrochloride to melt at 225 to 227° with decomposition. <sup>k</sup> The free base distills at 235-245° at 1 mm. Analysis on free base. <sup>l</sup> Crystallized from ether-alcohol mixture and washed with methyl ethyl ketone. <sup>m</sup> Crystallized from isopropyl alcohol and ethyl acetate. <sup>n</sup> Crystallized from chloroform and petroleum-hexane mixture. <sup>o</sup> Precipitated from ether with dry hydrogen chloride but not recrystallized. <sup>p</sup> Crystallized from acetone. <sup>q</sup> Crystallized from methanol and ether mixture. <sup>r</sup> After crystallization from isopropyl alcohol the free base melts at 143-145°. <sup>s</sup> The free base distills at 175° at 3 mm. <sup>t</sup> Hygroscopic. Analysis of hydrochloride was unsatisfactory. The free base distills 200-202° at 5 mm. Analysis of free base given. <sup>u</sup> Crystallized from water containing hydrochloric acid. <sup>v</sup> Crystallized from 48% hydrobromic acid and then from acetic acid. <sup>w</sup> Crystallized from water. <sup>x</sup> Free base. <sup>y</sup> *iso*-Form. <sup>z</sup> The free base distills at 92-100° at 1 mm. <sup>aa</sup> Then solidifies and remelts at 230-232°. <sup>bb</sup> Ionic chlorine only. <sup>cc</sup> A. Angeli and L. Alessandri, *Atti accad. Lincei*, **19**, I, 784-93; *C. A.*, **4**, 2634 (1910), report the formation of a compound HOCHPhCHPhNC<sub>6</sub>H<sub>10</sub>, m. p. 156-157°, but they do not describe a hydrochloride. R. E. Lutz, J. A. Freek and R. S. Murphey, *THIS JOURNAL*, **70**, 2016 (1948), report both racemates of this compound and report the m. p. of this isomer as 259-260° *in vacuo*. <sup>dd</sup> Emil Eidebenz, German Patent 671,786; *C. A.*, **33**, 6527 (1939). <sup>ee</sup> The free base distills at 130-149° at 0.1 mm. <sup>ff</sup> Melting points determined using a thermometer calibrated for 76-mm. immersion.

the reaction was complete, it was acidified with hydrochloric acid, distilled nearly to dryness *in vacuo*, and shaken with 500 ml. of water. The solid hydrochloride was collected on a filter, washed with ether and water, and dried; yield, 7.3 g., m. p. 224-227°. Recrystallization from ethanol did not raise the melting point.

N-Methyl- $\alpha$ -cyclohexylbenzylamine (29).—The method of preparation was similar to that previously described.<sup>5</sup> Cyclohexylmagnesium bromide was prepared from 14 g.

(0.6 mole) of magnesium, 100 g. (0.62 mole) of cyclohexyl bromide and 200 ml. of absolute ether. To this was added 24 g. (0.2 mole) of benzalmethylamine, and the mixture was refluxed for one and one-quarter hours. The base was distilled twice from a Claisen flask, b. p. 89° (0.135 mm.); yield, 10.2 g. (25.2%); *n*<sub>D</sub><sup>20</sup> 1.5287. It was converted to the hydrochloride by saturating its alcoholic solution with hydrogen chloride and diluting with absolute ether. The crystalline solid was boiled with isopropyl alcohol,

cooled, and filtered from a small amount of insoluble material. Dilution of the filtrate with absolute ether gave the pure hydrochloride, m. p. 251–253°.

**1-(4-Chlorophenyl)-2-phenyl-2-aminopropanol (30).**—This was prepared by the reaction of a Grignard reagent with an oxime.<sup>10</sup> In this case, 27 g. of 4-chloropropiophenone oxime<sup>11</sup> was heated to 140–145° for one-half hour with an excess of phenylmagnesium bromide. The products were separated and purified as described by Campbell, *et al.*<sup>10</sup>

**1,2-Di-*p*-methoxyphenylbutylamine (31).**—Ninety grams of  $\alpha$ -ethyldeoxyanisoin oxime<sup>12</sup> was dissolved in 3 l. of absolute methanol and treated with 300 g. of so-

(10) K. N. Campbell, B. K. Campbell and E. P. Chaput, *J. Org. Chem.*, **8**, 99 (1943).

(11) Collet, *Compt. rend.*, **126**, 1577 (1898); "Beilstein," **7**, 31.

(12) Peter P. T. Sah, *J. Chinese Chem. Soc.*, **13**, 111–118 (1946); *C. A.*, **41**, 5870 (1947).

dium. The resulting solution was boiled two hours and poured into 6 l. of 10% hydrochloric acid. The first crop of crystals was yellow, m. p. 60–80°. The second crop weighed 27 g., m. p. 252–258°. Treatment of the filtrate with alkali gave a gummy material, which, on treatment with 5% hydrochloric acid, crystallized to give 15 g., m. p. 200–225°. Crystallization of the second crop of crystals from dilute hydrochloric acid, then alcohol, and finally, distilled water, gave material, m. p. 269–271°.

### Summary

1. Thirty-one phenylalkylamines have been prepared and characterized for testing as analgesics.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE MUNICIPAL UNIVERSITY OF WICHITA]

## Derivatives of 2-Amino-4,8-dimethyl- and 4-Amino-3,8-dimethylquinoline<sup>1</sup>

BY DONALD E. EICHINGER<sup>2</sup> AND C. G. STUCKWISCH

In an attempt to find new types of compounds that exhibit antimalarial activity 2-substituted-4,8-dimethylquinolines and 4-substituted-3,8-dimethylquinolines were investigated.<sup>3</sup>

The key intermediate for the first series of compounds 2-chloro-4,8-dimethylquinoline (I), was prepared by the reaction of phosphorus oxychloride with 2-hydroxy-4,8-dimethylquinoline. The

the procedure of Roos.<sup>4</sup> 4-Chloro-3,8-dimethylquinoline (II) was prepared as described by Steck, *et al.*<sup>3</sup>

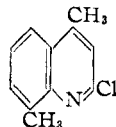
Compounds I and II were condensed with morpholine, piperidine, 1-hydroxymethylpropylamine and 4-diethylamino-1-methylbutylamine. Table I of the experimental section lists the properties of the compounds obtained.

TABLE I  
DERIVATIVES OF DIMETHYLQUINOLINES

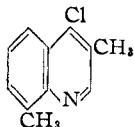
Compound	Yield, %	Solvent	M. p., °C.	Analyses, %					
				Carbon		Hydrogen		Nitrogen	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
2-Substituted-4,8-dimethylquinolines									
Piperidino	73	Ethanol	47	80.0	79.9	8.33	8.34	11.66	11.67
Morpholino	52	Ethanol	62	74.3	74.5	7.43	7.47	11.56	11.60
1-Hydroxymethyl-propylamino <sup>a</sup>	18	Benzene	163	73.7	73.6	8.20	8.19	11.48	11.65
4-Diethylamino-1-methylbutylamino <sup>a</sup>	31 <sup>b</sup>	" <sup>b</sup>		75.2	75.4	9.72	9.76	13.42	13.21
4-Substituted-3,8-dimethylquinolines									
Piperidino	65	Methanol	58	80.0	79.8	8.33	8.35	11.66	11.71
Morpholino	63	Methanol	72	74.3	74.2	7.43	7.44	11.56	11.63
1-Hydroxymethylpropylamino <sup>a</sup>	60	Bz-EtOH	129	73.7	73.6	8.20	8.26	11.48	11.56

<sup>a</sup> In these condensations phenol was added to the reaction mixture. The mixture was maintained at reflux temperature for twenty hours. <sup>b</sup> Distilled, 200° (2 mm.).

latter was obtained in essential accordance with



I



II

(1) Abstracted in part from a Master's Thesis by D. E. Eichinger.

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(3) Since the inception of this work in September, 1945, 3,8-dimethyl-4-dimethylamino-1-methylbutylaminoquinoline has been described by Steck, Hallock and Holland, *THIS JOURNAL*, **68**, 132 (1946).

### Experimental

**2-Chloro-4,8-dimethylquinoline (I).**—In a 250-ml. flask, equipped with an air condenser were placed 88 g. (0.51 mole) of 2-hydroxy-4,8-dimethylquinoline and 94 g. (0.61 mole) of freshly distilled phosphorus oxychloride. The mixture was maintained at 80 to 90° for two hours and was then poured into 500 ml. of water and 500 g. of cracked ice. The white precipitate was filtered off, dried and crystallized from 95% ethanol. The yield of white 2-chloro-4,8-dimethylquinoline, melting at 63°, was 93 g. or 96%.

*Anal.* Calcd. for C<sub>11</sub>H<sub>10</sub>NCl: N, 7.30; Cl, 18.51; Found: N, 7.46; Cl, 18.21.

**4-Chloro-3,8-dimethylquinoline (II).**—The sequence of reaction for the preparation of 4-chloro-3,8-dimethyl-

(4) Roos, *Ber.*, **21**, 624 (1888).