the dihydrochloride in ethyl acetate and was recrystallized twice from a mixture of alcohol–ether; m. p. 205–205.5°. Calcd. for $C_{25}H_{49}N_3Cl_2$: N, 9.08; Cl, 15.34. Found: N, 9.18; Cl, 15.76.

N,N-Diethyl-N'-(2,2-dibutylhexyl)-ethylenediamine.—A mixture of 21 g. (0.1 mole) of 2,2-dibutylhexylamine, 14 g. (0.1 mole) of diethylaminoethyl chloride and 11 g. of anhydrous sodium carbonate in 50 cc. of dry xylene was refluxed with stirring for sixty-five hours. The cooled reaction product was poured into water, the xylene layer separated, and the solvent removed *in vacuo*. The brown oily residue was distilled; yield 29 g.; b. p. 155–156° (2 mm.); $n^{23}D$ 1.4540. The analytical sample showed the following constants: b. p. 151–152° (1.5 mm.); $n^{23}D$ 1.4513. Calcd. for $C_{20}H_{44}N_2$: C, 76.82; H, 14.20; N, 8.97. Found: C, 76.71; H, 13.74; N, 9.26.

Acknowledgment.—We wish to express our appreciation to Dr. Richard Tislow and Mrs. Annette LaBelle of our Pharmacology Laboratory for the pharmacological data reported herein.

Summary

Replacement of the benzyl group in N'-benzyl-N'-(2-pyridyl)-N,N-dimethylethylenediamine by a highly branched aliphatic radical resulted in a considerable decrease in antihistaminic activity.

BLOOMFIELD, N. J. RECEIVED SEPTEMBER 9, 1948

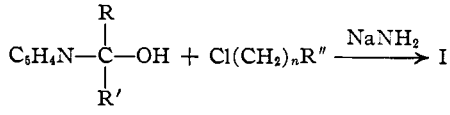
[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION OF SCHERING CORPORATION]

Pyridyl-Substituted Alkamine Ethers as Antihistaminic Agents[1]

BY NATHAN SPERBER, DOMENICK PAPA, ERWIN SCHWENK AND MARGARET SHERLOCK

Although Fourneau and co-workers[2] demonstrated that dialkylaminoalkylaryl ethers[3] possessed antihistaminic activity, these substances proved too toxic for general clinical use. Recently, a series of dialkylaminoalkylbenzhydryl ethers[4] have been reported[5] to be potent antihistaminic agents. One of the latter type of compounds, β-dimethylaminoethyl benzhydryl ether, is employed at present in anti-allergic therapy.

The extremely favorable change in therapeutic index which resulted from the replacement of the phenyl group by a pyridyl group[6] in N'-phenyl-N'-benzyl-N,N-dimethylethylenediamine seemed of sufficient interest to warrant the study of a similar substitution in the benzhydrylalkamine ether series. A number of substituted dialkylaminoalkylpyridylmethyl ethers of the general formula I (Table II) wherein R is a pyridyl radical, R' is alkyl, aryl or heterocyclic, R'' is hydrogen or a lower alkyl group, n is 2 or 3 and R''' is a dialkylamino group, were synthesized by the condensation of the appropriately substituted carbinols with dialkylaminoalkyl halides and sodium amide in toluene. In general, the yields of ethers varied from about 45–88%. In the case of (2-pyridyl)-(2-thienyl)-methylcarbinol, only 22% of the dimethylaminoethyl ether was obtained.



The requisite carbinols (Table I) were synthesized by the following three methods[7]: (I) the reaction of aldehydes with 2-pyridylmagnesium bromide as described by Overhoff and Proost[8]: (II) The condensation of picolinic acid and aromatic aldehydes and ketones to yield the secondary and tertiary pyridylarylcarbinols,[9] respectively; (III) tertiary carbinols were also prepared by the reaction of 2- or 3-acetylpyridine with aryl or aralkylmagnesium halides.

Although method I is reported to give 40–55% of the carbinols, we have not been able to duplicate these yields. Furthermore, this synthesis required the use of large volumes of solvent for extraction and, frequently, troublesome emulsions were encountered.

A more satisfactory method for the preparation of the secondary substituted 2-pyridylcarbinols is based on the decarboxylation of picolinic acid in the presence of an aromatic aldehyde at a temperature above 140° (Method II). The products of

(1) The major portion of this paper was presented in abstract before the Division of Medicinal Chemistry at the Chicago Meeting of the American Chemical Society, April 21, 1948. Similar amino ethers have been reported by Tilford, Van Campen and Shelton, abstract of Papers of 114th Meeting of the American Chemical Society, pg. 2K (August 31, 1948).

(2) Forneau and Bovet, *Arch. internat. de pharmacodyn. et de therap.*, **46**, 178 (1933); Staub, *Ann. Inst. Pasteur*, **63**, 400 (1939).

(3) 929F, 2-isopropyl-5-methylphenoxyethyldiethylamine; 1379F, 2-methyl-5-isopropylphenoxyethyldiethylamine; 1464F, 2-isopropyl-5-methylphenoxyethylpiperidine.

(4) Abstracts of the Atlantic City Meeting of the American Chemical Society, p. 50K (1946); Rieveschl, U. S. Patent 2,421,714, June 3, 1947.

(5) Loew, Kaiser and Moore, *J. Pharmacol. and Exp. Therap.*, **83**, 120 (1945); Loew and Kaiser, *Proc. Soc. Exper. Biol. and Med.*, **58**, 235 (1945).

(6) Huttrer, Djerassi, Beears, Mayer and Scholz, THIS JOURNAL, **68**, 1999 (1946).

(7) (a) Chichibabin oxidized 2-benzylpyridine to phenyl-2-pyridyl ketone (*J. Russ. Phys.-Chem. Soc.*, **33**, 701 (1901)). The latter was reduced to the corresponding carbinol with zinc dust and sodium ethoxide (*Ber.*, **37**, 1371 (1904)); (b) Emmert and Asendorf (*Ber.*, **72**, 1188 (1939)) have prepared several 2-pyridyl-substituted carbinols by the reaction of a ketone and mercuric chloride with pyridine and magnesium.

(8) Overhoff and Proost, *Rec. trav. chim.*, **57**, 179 (1938).

(9) Ashworth, Daffern and Hammick, *J. Chem. Soc.*, 809 (1939); Mislow, THIS JOURNAL, **69**, 2559 (1947).

TABLE I

CARBINOLS, RR'R"C—OH

R	R'	R"	Method	Yield,[a] %	M. p., °C.	B. p., °C.	Mm.	Formula	N Analyses, % Calcd.	Found
2-C_5H_4N	C_6H_5	H	I (II)	35 (49)	77–77.5[b]	133–138	1			
2-C_5H_4N	p-i-$C_3H_7C_6H_4$	H	I (II)	42.5 (24.5)	102.5–103	166–170	2	$C_{16}H_{17}ON$	6.16	6.35
2-C_5H_4N	p-$CH_3C_6H_4$	H	I (II)	34 (49)		146–152	1	$C_{13}H_{13}ON$	7.03	7.12
2-C_5H_4N	m-$CH_3C_6H_4$	H	I (II)	25 (29)	105–106			$C_{13}H_{13}ON$	7.03	7.17
2-C_5H_4N	p-$CH_3OC_6H_4$	H	I (II)	32 (33)	133–134[c]			$C_{13}H_{13}O_2N$	6.51	6.68
2-C_5H_4N	p-$(CH_3)_2NC_6H_4$	H	I	23		146–152	0.5	$C_{14}H_{16}ON_2$	12.27	12.75
2-C_5H_4N	3,4-$CH_2O_2C_6H_3$	H	I (II)	19 (26)	142–142.5			$C_{13}H_{11}O_3N$	6.11	6.27
2-C_5H_4N	o-ClC_6H_4	H	II	45	63–64	136–140	1	$C_{12}H_{10}ONCl$	6.38	6.39
2-C_5H_4N	p-ClC_6H_4	H	II	37	80–81			$C_{12}H_{10}ONCl$	6.38	6.28
2-C_5H_4N	3,4-$(OCH_3)_2C_6H_3$	H	II	2.5		180–185	1.5	$C_{14}H_{15}O_3N$	5.72	5.88
2-C_5H_4N	$C_6H_5CH_2$	H	I	9	104–105			$C_{13}H_{13}ON$	7.03	6 98
2-C_5H_4N	$C_6H_5CH_2CH_2$	H	I	20		148–152	1	$C_{14}H_{15}ON$	6.57	6.81
2-C_5H_4N	2-C_4H_3S	H	I	16.5		139	1	$C_{10}H_9OSN$	7.33	7.41
2-C_5H_4N	n-C_3H_7	H	I	34		94–98	1	$C_9H_{13}ON$	9.27	10.15
3-C_5H_4N	C_6H_5	H	I	36		180–182	2.5	$C_{12}H_{11}ON$	7.56	7.70
2-C_5H_4N	C_6H_5	CH_3	III (II)	76.5 (17)		133–136	0.5[d]	$C_{13}H_{13}ON$	7.03	7.27
2-C_5H_4N	p-ClC_6H_4	CH_3	II	13		134–138	0.5	$C_{13}H_{12}ONCl$	Cl, 15.18	15.15
2-C_5H_4N	C_6H_5	C_6H_5	II	14.5	105.5–106[e]					
2-C_5H_4N	2-C_5H_4N	CH_3	II	17	46–47	109–112	1	$C_{12}H_{12}ON_2$	13.99	13.89
2-C_5H_4N	2-C_4H_3S	CH_3	II	12	49–50			$C_{11}H_{11}OSN$	6.82	6.88
3-C_5H_4N	$C_6H_5CH_2$	CH_3	III	47		160–165	2	$C_{14}H_{15}ON$	6.57	6.51
3-C_5H_4N	C_6H_5	CH_3	III	60.5	92–93			$C_{13}H_{13}ON$	7.03	7.26

[a] Yields are based on a limited number of experiments and do not necessarily represent the maximum obtainable. [b] Ref. 9, m. p. 78°. [c] Ref. 9, m. p. 131.5°. [d] Ref. 9 described this compound as distilling at 152.5° (745 mm.); ref. 7b gives b. p. 301–303° and m. p. 32°. [e] Ref. 9, m. p. 105°.

this reaction are the desired carbinol, pyridine and carbon dioxide. Although the yields are reported to be rather low, the ease of operation and isolation of the carbinols renders the method a useful synthetic procedure. However, it appeared advisable to study the conditions for the preparation of a typical carbinol, since the published procedures make no mention of the effects of solvents or the ratio of reactants on yields.

Method I: $2BrC_5H_4N + C_2H_5Br + Mg \longrightarrow 2C_5H_4N—MgBr \xrightarrow{RCHO}$

Method II: $2\text{-}C_5H_4N—COOH + RCHO \longrightarrow C_5H_4N—\underset{R}{\underset{|}{C}}HOH$

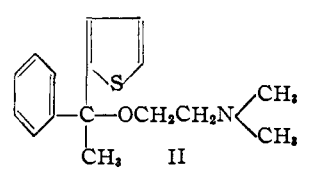
$2\text{-}C_5H_4N\text{-}COOH + RCOCH_3 \longrightarrow C_5H_4N—\underset{R}{\underset{|}{\underset{CH_3}{\underset{|}{C}}}}—OH$

Method III: $C_5H_4N—COCH_3 + RMgBr \longrightarrow$

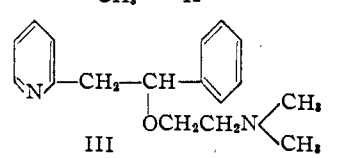
R = aryl or heterocyclic radical.

In the case of *p*-tolyl-2-pyridylcarbinol, the yield of carbinol is greatest when the ratio of aldehyde to picolinic acid is 6:1 and *p*-cymene at reflux temperature is used as solvent. Ashworth, *et al.*,[9] have used no solvent and a ratio of aldehyde to picolinic acid of 3:1 and 8:1 with no apparent increase in yield. It has been established that *p*-cymene is definitely superior to no solvent and to xylene. The optimum reaction time was found to be six hours and the yield of carbinol was not increased when the reaction was run for sixteen hours or when a nitrogen atmosphere was used.

In the course of this investigation, attempts to obtain 1-phenyl-1-(2-thienyl)-1-(β-dimethylaminoethoxy)-ethane (II) and 1-phenyl-1-(β-dimethylaminoethoxy)-2-(2-pyridyl)-ethane (III) were unsuccessful. In the case of II, instead of the expected tertiary carbinol, the Grignard reaction between bromobenzene and 2-acetylthiophene gave 1-phenyl-1-(2-thienyl)-ethylene, dehydration of the carbinol occurring notwithstanding precautions to remove traces of acid from the reaction product. The reaction of 1-phenyl-2-(2-pyridyl)-ethanol with β-dimethylaminoethyl chloride with sodium amide gave α-stilbazole and none of the expected ether, III.



II



III

Pharmacology.—The alkamine ethers listed in Table II have been tested for antihistaminic activity by the intravenous injections of lethal doses of histamine diphosphate one-half to one hour after the intravenous administration of the drug under test.

The most active compounds are the 2-pyridyl

TABLE II

ALKAMINE ETHERS $RR'R''—C—OCH_2CH_2N\langle^{R'''}_{R'''}$

No.	R	R′	R″	R‴	Yield,[a] %	B. p. °C.	Mm.	Formula	N Analyses, % Calcd.	Found	
1	2-C_5H_4N	C_6H_5	H	CH_3	82	158–162	1.5	$C_{16}H_{20}ON_2$	10.93	10.71	
2	3-C_5H_4N	C_6H_5	H	CH_3	69	149–153	1	$C_{16}H_{20}ON_2$	10.93	11.02	
3	2-C_5H_4N	p-i-$C_3H_7C_6H_4$	H	CH_3	84	165–167	0.5	$C_{19}H_{26}ON_2$	9.39	8.94	
4	2-C_5H_4N	p-$CH_3C_6H_4$	H	CH_3	88	156–160	1	$C_{17}H_{22}ON_2$	10.36	10.35	
5	2-C_5H_4N	m-$CH_3C_6H_4$	H	CH_3	72	155–159	0.5	$C_{17}H_{22}ON_2$	10.36	9.70	9.61[b]
6	2-C_5H_4N	p-$CH_3OC_6H_4$	H	CH_3	86	168–172	0.5	$C_{17}H_{22}O_2N_2$	9.78	9.71	
7	2-C_5H_4N	p-$(CH_3)_2N$-C_6H_4	H	CH_3	61	168–172	2.5	$C_{18}H_{25}ON_3$	14.03	13.46	13.34[b]
8	2-C_5H_4N	3,4-(—OCH_2O—)C_6H_3	H	CH_3	45	176–180	1	$C_{17}H_{20}O_3N_2$	9.34	9.05	
9	2-C_5H_4N	o-ClC_6H_4	H	CH_3	28	152–156	2	$C_{16}H_{19}ON_2Cl$	9.64	8.98	8.94[b]
10	2-C_5H_4N	p-ClC_6H_4	H	CH_3	47[c]	164–167	2	$C_{16}H_{19}ON_2Cl$	9.64	9.35	
11	2-C_5H_4N	$C_6H_5CH_2$	H	CH_3	63	138–142	0.5	$C_{17}H_{22}ON_2$	10.36	10.14	
12	2-C_5H_4N	$C_6H_5CH_2CH_2$	H	CH_3	56	178–180	0.5	$C_{18}H_{24}ON_2$	9.85	9.62	
13	2-C_5H_4N	2-C_4H_3S	H	CH_3	22	145	1	$C_{14}H_{18}ON_2$	10.68	11.03	
14	2-C_5H_4N	n-C_3H_7	H	CH_3	47	103–105	0.2	$C_{13}H_{22}ON_2$	12.60	12.61	
15	2-C_5H_4N	C_6H_5	H	C_2H_5	82	147–150	0.5	$C_{18}H_{24}ON_2$	9.85	9.97	
16	2-C_5H_4N	p-$CH_3C_6H_4$	H	C_2H_5	50[c]	162–165	1	$C_{19}H_{26}ON_2$	9.39	9.75	
17	2-C_5H_4N	p-$CH_3C_6H_4$	H	[e]	70	143–147	0.5	$C_{18}H_{24}ON_2$	9.88	9.80	
18	3-C_5H_4N	C_6H_5	CH_3	CH_3	87	160–161	1.5	$C_{17}H_{22}ON_2$	10.36	9.92	
19	2-C_5H_4N	C_6H_5	CH_3	CH_3	46	137–141	0.5	$C_{17}H_{22}ON_2$[d]	10.36	10.93	
20	2-C_5H_4N	p-ClC_6H_4	CH_3	CH_3	66	155–159	1	$C_{17}H_{21}ON_2Cl$	Cl, 11.63	11.24	
21	3-C_5H_4N	$C_6H_5CH_2$	CH_3	CH_3	76	170–173	1	$C_{18}H_{24}ON_2$	9.85	9.19	9.19[b]

[a] The yields are not calculated on the basis of recovered carbinol. [b] Low nitrogen analyses are due to traces of unreacted carbinol which could not be removed by repeated fractionation. [c] Some decomposition occurred during distillation. [d] At present in clinical use under the trade name "Decapryn." [e] The dialkylaminoalkyl residue is either $—CHCH_3N\langle^{CH_3}_{CH_3}$ (with CH_3 on the CH) or $—CH_2—CH(CH_3)—N\langle^{CH_3}_{CH_3}$ or both. Compare Schultz, Robb and Sprague, THIS JOURNAL, 69, 188 (1947); 69, 2454 (1947).

derivatives in which R′ is phenyl or an alkoxy, alkyl, halogen or dimethylamino substituted phenyl group, R″ is hydrogen or a methyl group and R‴ is methyl. These compounds, group I, (1, 3, 4, 5, 6, 7, 10, 19 and 20) have exhibited antihistaminic activity comparable to that of the presently available preparations. The oral LD/50 in mice was approximately 300–400 mg./kg.

Lower antihistaminic activity is exhibited by the 3-pyridyl compounds (2, 18 and 21) and the 2-pyridyl compounds wherein R′ is 3,4-methylenedioxybenzene (8), benzyl (11), phenethyl (12), 2-thienyl (13), n-propyl (14); or wherein R″ is C_2H_5 (15 and 16). Variations in the length of the carbon chain of the ether also result in decreased potency (17). In general, these compounds possess $^1/_5$ to $^1/_{100}$ the activity of the group I compounds. A detailed pharmacological report will appear elsewhere.

Experimental

Method I. 2-Pyridyl-p-isopropylphenylcarbinol.[8]—In a one-liter, three-necked flask equipped with a Hershberg tantalum stirrer, condenser and dropping funnel, there were placed 19.2 g. (0.8 mole) of magnesium turnings and 200 cc. of anhydrous ether. To the stirred mixture was added 20 g. (0.2 mole) of ethyl bromide. After the ethyl bromide had reacted, 64 g. (0.4 mole) of 2-bromopyridine was added dropwise at a rate which produced rapid reflux. The suspension was refluxed and stirred for an additional three hours. To the brown reaction mixture was added 89.5 g. (0.6 mole) of p-isopropylbenzaldehyde in 100 cc. of ether and the mixture was refluxed for ten hours. After decomposing the complex with cold, dilute hydrochloric acid, the aqueous acid layer was separated, made alkaline with gaseous ammonia and extracted with ether. The ether layer was dried over sodium sulfate, filtered, the ether removed and the residue distilled.

Method II. 2-Pyridyl-p-tolylcarbinol[9].—In a five-liter, three-necked flask equipped with a stirrer, condenser and nitrogen inlet tube, there were placed 100 g. of picolinic acid, 600 g. of p-tolualdehyde and 600 cc. of p-cymene. The reaction mixture was refluxed and stirred for six hours under nitrogen. The initial vigorous evolution of carbon dioxide subsided within a few hours. The solution was cooled and extracted with several portions of dilute hydrochloric acid. The aqueous acid layer was made alkaline with gaseous ammonia and the oil which separated was extracted with ether. The alkamine ether was isolated as described under Method I.

Method III. 2-Pyridylphenylmethylcarbinol.—In a 500-cc., three-necked flask, equipped with a stirrer, condenser and dropping funnel, there were placed 200 cc. of anhydrous ether and 4.4 g. (0.18 mole) of magnesium turnings. To the stirred mixture was added dropwise 28.2 g. (0.18 mole) of bromobenzene in 50 cc. of ether. The reaction mixture was then stirred and refluxed for one hour. After cooling the mixture, 20 g. (0.17 mole) of 2-acetylpyridine was added and a heavy white precipitate separated. After refluxing for several hours, the reaction mixture was decomposed with dilute hydrochloric acid and ice. The acid layer was separated, made alkaline with gaseous ammonia and extracted with ether. Isolation of the alkamine ether was carried out as described under Method I.

The alkamine ethers listed in Table II were prepared essentially as described for phenyl-2-pyridylmethyl-β-

N,N-dimethylaminoethyl ether (19): In a 500-cc., three-necked flask equipped with a stirrer, condenser and dropping funnel, containing a suspension of sodium amide (from 6.74 g. (0.29 mole) of sodium) in 250 cc. of dry xylene, there was added cautiously at 0° 53 g. (0.286 mole) of phenyl-2-pyridylmethylcarbinol. A vigorous evolution of ammonia occurred and the resulting deep blue reaction mixture was heated for several hours on the steam-bath. Then 32.5 g. (0.30 mole) of β-N,N-dimethylaminoethyl chloride was added and the reaction mixture heated for approximately eighteen hours on the steam-bath. During this time, the deep blue color of the sodium salt of the carbinol was discharged and a turbid brown mixture resulted. The excess sodium amide was decomposed with water, the xylene layer was separated and, after drying, was evaporated *in vacuo*. The crude alkamine ether was fractionated.

The following procedures were used in an attempt to secure ethers II and III. To phenylmagnesium bromide (48.7 g. bromobenzene) in 150 cc. ether, there was added 37.8 g. of 2-acetylthiophene. The reaction product yielded 23.3 g. of a pale yellow liquid, b. p. 100–108° (0.5 mm.).

Anal. Calcd. for $C_{12}H_{10}S$: C, 77.35; H, 5.41. Found: C, 77.26; H, 5.44. The residue from the distillation yielded 13.1 g. of a viscous material, b. p. 185–245 (0.5 mm.) which resinified on standing.

To a sodium amide suspension, from 1.2 g. of a sodium in 250 cc. of toluene, there was added at room temperature 10 g. of 1-phenyl-2-(2-pyridyl)-ethanol. The reaction mixture was heated with stirring on the steam-bath for two hours and then 9 g. of β-dimethylaminoethyl chloride was added. The condensation was carried out in the usual manner and the product distilled; yield 8.4 g.; b. p. 158–162° (2.5 mm.); m. p. 90–91° after recrystallization from aqueous ethanol, mixed m. p. with an authentic sample of α-stilbazole, 90–91°.

Acknowledgment.—We are grateful to Dr. Richard Tislow and Mrs. Annette LaBelle for the pharmacological data reported herein.

Summary

A series of pyridyl-substituted alkamine ethers has been synthesized from pyridyl substituted carbinols and dialkylaminoalkyl halides. In general, the 2-pyridyl substituted alkamine ethers showed a high order of antihistaminic activity whereas the corresponding 3-pyridyl compounds were relatively less active.

BLOOMFIELD, N. J. RECEIVED SEPTEMBER 15, 1948

[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

Quinolines. VII. Some 3-Methylquinolines

BY EDGAR A. STECK AND LOUIS L. HALLOCK[1]

Potential antimalarials of the 4-amino-3-methylquinoline type have been the subject of considerable investigation in these laboratories.[2-6] The bulk of these studies[2,5] was concerned with the influence of the variation of substituents in the benzenoid moiety upon the schizontocidal action of 4-(4-diethylamino-1-methylbutylamino)-3-methylquinoline derivatives. In the present contribution there are presented data relating to the preparation of 4-(4-diethylamino-1-methylbutylamino)-7-ethoxy-3-methylquinoline and certain experiences in the synthesis of other 3-methylquinolines which were terminated prior to completion because other work intervened.

The preparation of 4-chloro-7-ethoxy-3-methylquinoline, required for reaction with 4-diethylamino-1-methylbutylamine, was accomplished by a modification of the Conrad-Limpach synthesis.[2d] In the cyclization of the anil from 3-phenetidine and ethyl α-ethoxalylpropionate, only one quinoline ester appeared to be formed (*cf.* ref. 2c, d and 5), as in the case of the related methoxy series.[7] The structure of the series (notice Table I) could not be proved unequivocally, for several attempts to oxidize[2c,d] the ethoxy-4-hydroxy-3-methylquinoline or related 2-carboxylic acid gave only 3-phenetidine. There was no comment as to difficulty in the proof of structure of the 7-methoxy analog by oxidation,[7] but the facile decarboxylation of several anthranilic acids has been recorded in the literature recently,[8,9] including 4-methoxyanthranilic acid. The 7-position is assigned to the ethoxy group on the basis that only one product resulted from the pyrolytic cyclization (*cf.* ref. 7) and the ease with which the oxidation product decarboxylated to 3-phenetidine (*cf.* ref. 9).

The work on 3,5/7-dimethylquinoline derivatives was halted when it was learned that Hauser, *et al.*,[7] were engaged in similar studies. 3-Toluidine was employed as the starting material in the Conrad-Limpach synthesis, and the preparation discontinued at the 4-chloro-3,5/7-dimethylquinoline stage. The structure of the series, shown in Table I, was proven by the catalytic dehalogenation of one of the 4-chloroquinoline derivatives to the corresponding dimethylquinoline, previously prepared by Manske.[10] It was of interest that the lower-melting isomer of the 4-chloroquinoline type, here an oil, was the one bearing a methyl group in position 7 (*cf.* ref. 5).

(1) Present address: Commercial Solvents, Inc., Terre Haute, Ind.

(2) Steck, Hallock and Holland, THIS JOURNAL, **68**, (a) p. 129 (1946), (b) p. 132, (c) p. 380, (d) p. 1241.

(3) Huber, Bair, Laskowski, Jackman and Clinton, *ibid.*, **68**, 322 (1946).

(4) Kwartler and Lucas, *ibid.*, **68**, 2395 (1946).

(5) Steck, Hallock, Holland and Fletcher, *ibid.*, **70**, 1012 (1948).

(6) Steck, Hallock and Suter, *ibid.*, **70**, 4063 (1948).

(7) Hauser and co-workers, *ibid.*, **68**, 1232 (1946).

(8) Surrey and Cutler, *ibid.*, **68**, 2570 (1946).

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