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.[10] In this case, 27 g. of 4-chloropropiophenone oxime[11] 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.*[10]

1,2-Di-*p*-methoxyphenylbutylamine (31).—Ninety grams of α-ethyldesoxyanisoin oxime[12] was dissolved in 3 l. of absolute methanol and treated with 300 g. of sodium. 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.

KANSAS CITY, MISSOURI

RECEIVED[13] MAY 28, 1949

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[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).

[13] Original manuscript received June 17, 1948.

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

Derivatives of 2-Amino-4,8-dimethyl- and 4-Amino-3,8-dimethylquinoline[1]

BY DONALD E. EICHINGER[2] 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.[3]

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 latter was obtained in essential accordance with the procedure of Roos.[4] 4-Chloro-3,8-dimethylquinoline (II) was prepared as described by Steck, *et al.*[3]

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.

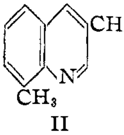
TABLE I

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[a]	18	Benzene	163	73.7	73.6	8.20	8.19	11.48	11.65
4-Diethylamino-1-methylbutylamino[a]	31[b]	[b]		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[a]	60	Bz–EtOH	129	73.7	73.6	8.20	8.26	11.48	11.56

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

I



II

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 $C_{11}H_{10}NCl$: 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-

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[1] Abstracted in part from a Master's Thesis by D. E. Eichinger.

[2] Present address: E. I. Du Pont de Nemours & Co., Philadelphia, Pennsylvania.

[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)

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

quinoline has been described in the literature.[8] Our yields and melting points agreed essentially with those reported.

Derivatives of Dimethylquinolines.—The compounds described in Table I were prepared by refluxing the chloro compound with an excess of the appropriate amine as the solvent. The reflux time was eight to ten hours. The reaction mixture was then poured on ice. The 4-diethylamino-1-methylbutylamino derivative was extracted from the water with ether and was purified by distillation; whereas the solid piperidino, morpholino and 1-hydroxymethylpropylamino derivatives were filtered off and crystallized.

Summary

1. 2-Chloro-4,8-dimethylquinoline has been prepared.

2. Some derivatives of 2-amino-4,8-dimethylaminoquinoline and 4-amino-3,8-dimethylquinoline are described.

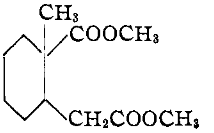
WICHITA, KANSAS RECEIVED APRIL 12, 1949

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

Reduction of a Diester to a Hydroxyester by Lithium Aluminum Hydride. Application to the Construction of Rings

BY W. E. BACHMANN AND ANDRE S. DREIDING[1]

No instance of the reduction of one of two ester groups by lithium aluminum hydride has been reported. Nystrom and Brown were unable to reduce one of the two primary carboxy groups of sebacic acid and its half ester at the boiling point of ether and suggested experimentation at lower temperatures.[2] We were interested in reducing selectively the primary ester group of the dimethyl ester of *cis*-2-methyl-2-carboxycyclohexaneacetic acid (I) to the alcohol (II) from which, after a malonic ester synthesis and cyclization, *cis*-9-methyl-1-decalone (III) could be obtained.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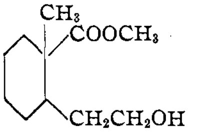
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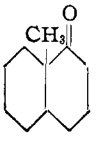
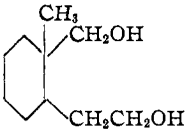

III


IV

Accordingly we examined the reduction of the diester (I) with an amount of lithium aluminum hydride sufficient to reduce only one ester group at low temperatures. Below −15° no visible change occurred. When the reaction mixture was kept near −15° the reagent was used up in reducing the primary carbomethoxy group to yield *cis*-β-2-methyl-2-carbomethoxycyclohexaneëthanol (II). The crude product was converted to the bromoester by the action of phosphorus tribromide. Condensation with sodiomalonic ester followed by hydrolysis and decarboxylation yielded *cis*-γ-2-methyl-2-carboxycyclohexanebutyric acid. Its dimethyl ester underwent the Dieckmann cyclization, hydrolysis, and decarboxylation to give *cis*-9-methyl-1-decalone (III) in a 15% over-all yield from I. These reactions represent a new synthesis of the bicyclic ketone (III) from the diester (I) and the procedure may prove to be generally applicable for the construction of rings since the starting acetic esters are frequently available through the Reformatsky reaction or malonic ester synthesis. Recently we described the preparation of the ketone (III) from the ester (I) through two successive Arndt–Eistert reactions followed by cyclization.[3]

Reduction of the diester (I) with sufficient lithium aluminum hydride to reduce both ester groups yielded *cis*-β-2-methyl-2-hydroxymethylcyclohexaneëthanol (IV). The same product (IV) was obtained when the diester (I) was treated with an excess of sodium in boiling ethanol.

Experimental

Reduction of the Diester (I) to the Hydroxyester (II).—A 0.15-g. piece of lithium aluminum hydride (Metal Hydrides Inc., Beverly, Massachusetts) was softened by allowing it to rest in 15 cc. of boiling anhydrous ether for twenty minutes, while excluding moisture and carbon dioxide. It was broken up with a stirring rod and the resulting supension was refluxed again for twenty minutes. The remaining undissolved particles were crushed and brought into solution almost completely by boiling for another twenty minutes. To the solution, cooled to −60° in a Dry Ice–acetone-bath, a solution of 1.8 g. of the dimethyl ester of *cis*-2-methyl-2-carboxycyclohexaneacetic acid (I, made from the corresponding diacid[4] by esterification with diazomethane) in 10 cc. of ether was added in small portions so that the temperature did not rise above −40°. The colorless solution, which contained only a small amount of undissolved solids, stood at −60° for five hours and was allowed to warm up slowly. At −15° a colorless gelatinous precipitate appeared. The mixture was kept at −15 to −10° for twenty minutes by reinserting the flask in the cold bath from time to time with swirling. After standing at room temperature for three hours, a small amount of 10% sodium hydroxide and then excess hydrochloric acid was added. The ethereal layer was washed with a saturated sodium chloride solution and concentrated, and the crude residue was evaporatively distilled. The colorless camphoraceous oil (0.83 g. or 53%, presumably *cis*-β-2-methyl-2-carbomethoxycyclohexaneëthanol, II), which was collected at 70–80° (0.4 mm.), was

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[1] Alfred H. Lloyd Postdoctoral Fellow in the Horace H. Rackham School of Graduate Studies 1947/1948.

[2] Nystrom and Brown, THIS JOURNAL, **69**, 2548 (1947).

[3] Bachmann and Dreiding, *J. Org. Chem.*, **13**, 317 (1948).

[4] Chuang, Tien and Huang, *Ber.*, **68**, 866 (1935); Bachmann and Kushner, THIS JOURNAL, **65**, 1963 (1943).