plished by passing methylcyclopentane over silica gel.[4]

The following table shows the inhibiting effect of benzene upon the isomerization of methylcyclopentane promoted by *s*-butyl bromide. The experiments were carried out by a general procedure described previously[3]; the reaction temperature was 25° and the duration of each experiment was two hours. On the average about 0.04 mole of methylcyclopentane was used in each experiment.

TABLE I

EFFECT OF BENZENE UPON THE ISOMERIZATION OF METHYLCYCLOPENTANE

Expt.	Reagents used: moles per 100 moles of methylcyclopentane AlBr₃	HBr	*s*-C₄H₉Br	Benzene	Cyclohexane formed, mole %
1	2	1.0	0.0	0.000	0
2	2	0.9	.1	.000	51
3	2	.9	.1	.022	22
4	2	.9	.1	.072	5
5	2	.9	.1	.140	3
6	2	1.0	.0	.140	0

The concentration of benzene in methylcyclopentane was determined by ultraviolet analysis. Experiment 4 was made by the addition of benzene to a purified sample of methylcyclopentane.

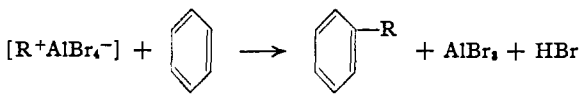
The inhibiting effect of benzene upon the isomerization, which was also observed to occur in the case of *n*-pentane,[5] is probably due to the ease with which the benzene reacts with the chain initiator. The ultraviolet absorption spectra taken of the hydrocarbons obtained from experiment 5 after removal of the catalyst by washing show that probably a mono-alkylbenzene was formed during the reaction. The absorption spectrum of the methylcyclopentane containing 0.14% of benzene and that of the reaction product was taken. The spectrum of the product showed a slight peak at 258.5 mμ where *s*-butylbenzene has a strong absorption band.

In expt. 3 the benzene caused only a partial inhibition of isomerization. This is not surprising since the molal ratio of *s*-butyl bromide to benzene used was over four, and the alkylation usually does not proceed beyond the formation of a tributylbenzene. There was therefore still some *s*-butyl bromide left to act as a chain initiator.

It was also noticed that in the experiments 3, 4, and 5 where benzene and *s*-butyl bromide were used an oily-yellow layer deposited on the walls of the reaction tube; in all the other experiments the product was homogeneous and free of color.[6] It is probable that the alkylbenzenes or cycloalkylbenzenes produced in the reaction formed a complex with the aluminum bromide and hydrogen bromide, similar to the type reported by Norris and Rubinstein.[7]

The inhibition of the isomerization of methylcyclopentane by benzene is in accordance with the proposed chain mechanism of isomerization.[1,8]

In the presence of benzene the chain may break by the reaction



R^+ may correspond to the carbonium ion obtained from the original olefin or from the product resulting from an exchange reaction between methylcyclopentane or cyclohexane formed and the *s*-butylcarbonium ion.

(4) B. J. Mair and A. F. Forziati, *J. Research Natl. Bur. Standards*, **32**, 151, 165 (1944).

(5) J. M. Mavity, H. Pines, R. C. Wackher, and J. A. Brooks, *Ind. Eng. Chem.*, **40**, 2374 (1948).

(6) In the last paper of this series[3] it was reported that the isomerization of methylcyclopentane to cyclohexane was usually accompanied by the formation of an oily layer even though the methylcyclopentane used did not contain any traces of benzene. It was observed now that when methylcyclopentane is further purified by passing it over silica gel certain impurities not detectable by spectrographic analysis and responsible for the formation of an oily layer are removed.

(7) J. F. Norris and D. Rubinstein, THIS JOURNAL, **61**, 1163 (1939).

(8) H. S. Bloch, H. Pines and L. Schmerling, *ibid.*, **68**, 153 (1946).

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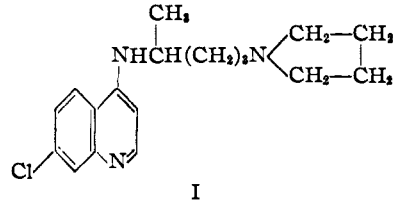
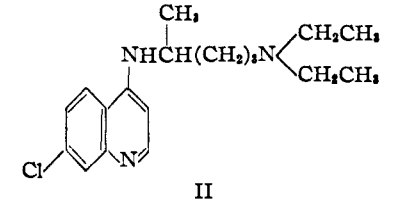
Synthesis of 7-Chloro-4-[1-methyl-(1-pyrrolidyl)-butylamino]-quinoline

BY ROBERT H. REITSEMA AND JAMES H. HUNTER

Studies on the effects resulting from an exchange of a pyrrolidyl group for a dialkylamino substituent in various chemotherapeutic agents[1] has now been extended briefly into the field of antimalarials. The synthesis of 7-chloro-4-[1-methyl-4-(1-pyrrolidyl)-butylamino]-quinoline (I), the pyrrolidyl analog of Chloroquine (II) was undertaken in consequence of the utility reported[2] for the latter in the control of malaria.



I



II

(1) (a) Wright, Kolloff and Hunter, THIS JOURNAL, **70**, 3098 (1948); (b) Reid, Wright, Kolloff and Hunter, *ibid.*, **70**, 3100 (1948); (c) Reitsema and Hunter, *ibid.*, in press.

(2) Wiselogle, "A Survey of Antimalarial Drugs," Vol. I, J. W. Edwards, Ann Arbor, 1946, pp. 388–392.

Preparation of 5-(1-pyrrolidyl)-2-aminopentane (III) from ethyl acetoacetate and β-1-pyrrolidylethyl chloride[1a] was patterned after the synthesis used for noval diamine.[3] Alkylation of III with 4,7-dichloroquinoline occurred smoothly to give the desired aminoquinoline (I).

In suppressive tests on *p. gallinaceum* in the chick, the order of activity and toxicity of I was analogous to that of Chloroquine.[4]

Experimental

5-(1-Pyrrolidyl)-3-carbethoxypentanone-2.—A solution of 400 g. (2.35 moles) of pyrrolidylethyl chloride hydrochloride in 200 ml. of water was treated with Nuchar C twice. The resulting light yellow solution was covered with 200 ml. of benzene, cooled to 5° and cold 50% potassium hydroxide was added with stirring and cooling below 12°. The upper organic layer was separated and the aqueous layer extracted twice with 100-ml. portions of benzene. Titration of a sample of the combined layers indicated 2.25 moles of base in solution or 96% of theory.

The sodium salt of 172 g. of acetoacetic ester in 1 l. of dry benzene was prepared with 26.0 g. of sodium sand. After addition of the ester was complete the mixture was boiled under reflux for one hour. One half of the above benzene solution of pyrrolidylethyl chloride was added dropwise. No reaction was apparent and the mixture was boiled under reflux for ten hours. After two hours nearly all the material was in solution.

5-Pyrrolidylpentanone-2.—To the above solution was added dilute sulfuric acid (from 160 ml. of water, 140 g. of ice, and 75 ml. of sulfuric acid). When about two-thirds of the acid had been added the solution was filtered and the layers separated. The remainder of the acid was used to dissolve the solid on the filter and to wash the benzene layer. The combined aqueous layers were washed with 100 ml. of benzene. The benzene was removed by distillation and the residual solution was boiled under reflux for seventeen hours. To the cooled solution was added 430 ml. of 30% sodium hydroxide with cooling and an organic layer of 184 g. was removed. The aqueous layer was extracted three times with 100-ml. portions of benzene. The dried organic layer was distilled to give 129 g. (74%) of material boiling at 92–98° (11–13 mm.). Redistillation of this gave a fraction which weighed 98.2 g.; b. p. 93–95° (11 mm.), $n^{20}D$ 1.4589.

Anal. Calcd. for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02. Found: C, 70.10; H, 11.07; N, 8.35.

5-Pyrrolidyl-2-aminopentane.—A solution of 88.1 g. (0.568 mole) of 5-pyrrolidylpentanone-2, in a mixed solvent consisting of 100 ml. of dry ammonia and 100 ml. of dry methanol was reduced in two portions in the presence of Raney nickel catalyst. Reduction was complete after one and one-third to two hours at 100°. After filtration and removal of solvent the residue was distilled to give 86.8 g. of 5-pyrrolidyl-2-aminopentane, b. p. 92–97° (11–12 mm.), $n^{20}D$ 1.4665. This was purified through the dithiocarbamate[5] to give a product which boiled at 93–94° (11 mm.), $n^{20}D$ 1.4674.

Anal. Calcd. for $C_9H_{20}N_2$: C, 69.17; H, 12.89. Found: C, 69.45; H, 12.44.

The picrate after recrystallization from ethanol melted at 148–149°.

Anal. Calcd. for $C_{21}H_{26}N_8O_{14}$: C, 41.04; H, 4.27. Found: C, 41.06; H, 4.27.

7-Chloro-4-[1-methyl-4-(1-pyrrolidyl)-butylamino]-quinoline.—A mixture of 29.0 g. (0.147 mole) of 4,7-dichloroquinoline and 50.0 g. (0.322 mole) of 5-pyrrolidyl-2-aminopentane was heated with stirring for six hours at 160–170°. The cold mixture was taken up in 120 ml. of 50% acetic acid with cooling. After addition of 100 ml. of ether, 140 ml. of 30% sodium hydroxide was added to give a strongly basic solution. The mixture was shaken, the ether layer separated, and the aqueous layer was extracted with three 100-ml. portions of ether. The combined ether extracts were dried over magnesium sulfate. After removal of the solvent, 20.1 g. of an oil boiling at 93° (11 mm.) was obtained leaving a residue of 45.7 g. (98%). A portion (31 g.) of this dark green fluorescent residue was taken up in 100 ml. of hot methylcyclohexane. Upon cooling 28 g. of yellow solid, m. p. 98–107°, was obtained. Three recrystallizations from methylcyclohexane gave some oily solid as a first precipitate and 13 g. of white 7-chloro-4-[1-methyl-4-(1-pyrrolidyl)-butylamino]-quinoline, m. p. 110–111°.

Anal. Calcd. for $C_{18}H_{24}N_3Cl$: C, 68.01; H, 7.61; N, 13.22. Found: C, 68.11; H, 7.52; N, 12.68.

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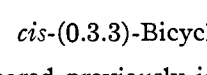
(3) Research and Manufacturing at I. G. Farbenindustrie; British Intelligence Objectives Subcommittee, Appendix 9, Processes 3–7.

(4) We wish to express our appreciation to the National Institute of Health and to William Longenecker for these pharmacological data.

(5) Jones, *Ind. Eng. Chem., Anal. Ed.*, 7, 431 (1944).

The Preparation and Properties of *cis*-(0.3.3)-Bicycloöctane

BY A. W. RYTINA,[1] ROBERT W. SCHIESSLER AND FRANK C. WHITMORE[2]

cis-(0.3.3)-Bicycloöctane  was prepared previously in very small quantity by Linstead and Cook[3] by heating the semicarbazone of *cis*-α-(0.3.3)bicycloöctanone with potassium hydroxide at 200–210°. A small-scale trial of this method by the present workers resulted in a poor (less than 40%) yield of hydrocarbon, therefore the conversion of the ketone to hydrocarbon was accomplished by the modified Wolff–Kishner reaction.[4] A 68% yield of bicycloöctane was realized, based on carefully purified material.

The hydrocarbon was purified by fractional distillation through a 25-plate helix-packed column, and the following properties determined.

°C.	Density,[a] g./ml.	Viscosity,[b] cp.
0.0	0.8863	2.839
20.0	.8695	1.859
37.8	.8543	1.350
60.0	.8353	0.9598

B. p.: 136.5° (±0.2°) at 738.3 mm.

M. p.: *ca.* −49° (much difficulty was encountered with glass formation)

$n^{20}D$: 1.4622

Mol. refraction (20°C.): found 34.85; calcd. 34.76

[a] ±0.0001; corrected for air buoyancy. [b] ±0.2%.

Experimental

Following the method of Linstead,[3] a total of 300 g. of pure *cis*-α-(0.3.3)bicycloöctanone was prepared from indene by hydrogenation to hydrindene, sulfonation, fusion with potassium hydroxide of the resultant 5-hydrin-

(1) Present address: Rohm and Haas, Philadelphia, Pa.

(2) Deceased.

(3) Linstead and Cook, *J. Chem. Soc.*, 946 (1934).

(4) Whitmore, Herr, Clarke, Rowland and Schiessler, THIS JOURNAL, 67, 2059 (1945).