The solution was then boiled for fifteen minutes, after which the rotation was 0.

Due to the deep color of the sodium salt, no rotation could be observed on account of the extreme dilution which was necessary before light would pass through the tube.

Summary

1. 2,4,2′,4′-Tetracarboxy-6,6′-diphenyl-3,3′-dipyridyl has been prepared by the oxidation of 1,10-dicarboxy-3,8-diphenyl-4,7-phenanthroline. This in turn was prepared by the condensation of *p*-phenylenediamine with benzaldehyde and pyruvic acid.

2. The dipyridyl was resolved through the brucine salt. The active acid was readily racemized by warming for a short time in ethyl alcohol.

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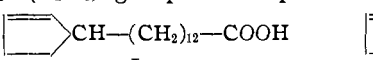
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

THE PREPARATION OF VARIOUS OMEGA-CYCLOHEXYL ALKYL AMINES AND THEIR BACTERICIDAL ACTION TO MYCOBACTERIUM LEPRAE. XXII[1]

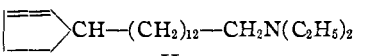
BY GERALD H. COLEMAN AND ROGER ADAMS

RECEIVED DECEMBER 21, 1931 PUBLISHED MAY 7, 1932

In one of the earlier papers[2] describing the preparation and bactericidal properties of various aliphatic acids, it was demonstrated in the case of chaulmoogric acid (I) that the carboxyl group could be replaced by a $-CH_2N(C_2H_5)_2$ group and the product (II) still had bactericidal properties.

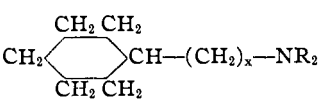


I



II

The present investigation involved the synthesis of a series of ω-cyclohexyl-alkyl tertiary amines of varying molecular weight and of the general formula (III).

III  $R = C_2H_5$, C_3H_7 or C_4H_9; $x = 1$ to 5

These compounds correspond essentially to the series of acids described in earlier papers.

The bacteriological study was made with the same strain of *Mycobacterium leprae* used with the acids. The amines were made into the hydrochloride salts and tested in the same manner as the sodium salts of the acids.[1b] The table (I) of results is given below.

The conclusions are very definite. The bactericidal value is dependent, in part at least, on molecular weight just as in the acids. It is obvious

[1] For the last three papers in this series see (a) Stanley, Coleman, Greer, Sacks and Adams, *J. Pharmacol.* (June, 1932); (b) Stanley and Adams, THIS JOURNAL, **54**, 1548 (1932); (c) Greer and Adams, *ibid.*, **52**, 2540 (1930).

[2] Sacks and Adams, *ibid.*, **48**, 2395 (1926).

TABLE I

CYCLOHEXYL SUBSTITUTED AMINES, $C_6H_{11}(CH_2)_xNR_2 \cdot HCl$

	Dilution of hydrochloride salts in thousands												
	5	10	20	22	27	35	50	70	80	100	125	155	200
$C_6H_{11}NH_2 \cdot HCl$	+	+	+	+	+	+	+	+	+	+	+	+	+
$C_6H_{11}CH_2NH_2 \cdot HCl$	+	+	+	+	+	+	+	+	+	+	+	+	+
$C_6H_{11}(CH_2)_2NH_2 \cdot HCl$	±	+	+	+	+	+	+	+	+	+	+	+	+
$C_6H_{11}N(C_2H_5)_2 \cdot HCl$	+	+	+	+	+	+	+	+	+	+	+	+	+
$C_6H_{11}CH_2N(C_2H_5)_2 \cdot HCl$	+	+	+	+	+	+	+	+	+	+	+	+	+
$C_6H_{11}(CH_2)_3N(C_2H_5)_2 \cdot HCl$	−	+	+	+	+	+	+	+	+	+	+	+	+
$C_6H_{11}(CH_2)_4N(C_2H_5)_2 \cdot HCl$	−	−	±	+	+	+	+	+	+	+	+	+	+
$C_6H_{11}(CH_2)_5N(C_2H_5)_2 \cdot HCl$	−	−	−	−	−	+	+	+	+	+	+	+	+
$C_6H_{11}(CH_2)_6N(C_2H_5)_2 \cdot HCl$	−	−	−	−	−	−	−	−	−	−	+	+	+
$C_6H_{11}(CH_2)_4N(C_3H_7)_2 \cdot HCl$	−	−	−	−	−	−	±	±	+	+	+	+	+
$C_6H_{11}(CH_2)_4N(C_4H_9)_2 \cdot HCl$	−	−	−	−	−	−	±	−	±	+	+	+	+
$C_6H_{11}(CH_2)_5N(C_3H_7)_2 \cdot HCl$	−	−	−	−	−	−	−	−	−	−	−	±	+

from the table that the molecules containing fifteen to eighteen carbon atoms show marked bactericidal action, but the action is insignificant or nil in the smaller molecules. The distribution of the carbon atoms in the cyclohexylalkyl residue or in the alkyl groups has, apparently, very little effect.

Presumably the proper combination of physical properties exists in these amine salts as in the salts of the acids. From these results it would appear that the carboxyl group and the amine group in bactericidal compounds of equal molecular weight may be interchangeable, though the bactericidal value of the amines is less than in the corresponding acids.

The amines were prepared by condensing the proper bromide with the secondary amines and the hydrochlorides were formed by precipitation with dry hydrogen chloride from a dry ether solution of the bases. The intermediate bromides were the same as those used in the synthesis of ω-cyclohexylalkyl aliphatic acids.[3]

Experimental

Cyclohexylamine was prepared according to the method of Hiers and Adams,[4] b. p. 132–133°; hydrochloride salt, after crystallization from chloroform and petroleum ether, m. p. 202°.

Cyclohexylmethylamine,[5] b. p. 159.5–160°; hydrochloride salt after crystallization from chloroform and petroleum ether, m. p. 252–253°.

β-Cyclohexylethylamine[5] was prepared from cyclohexylethyl bromide. A mixture of 10 g. of cyclohexylethyl bromide and 9.8 g. of potassium phthalimide was refluxed in a 100-cc., round-bottomed flask at 230–250° for seven hours. The mixture was cooled and extracted with 125 cc. of absolute alcohol. After evaporating the alcohol, the product was refluxed for one-half hour with 50 cc. of 10% potassium hydroxide solution and then for one-half hour after the addition of 10 cc. of concentrated hydrochloric acid.

[3] Hiers and Adams, THIS JOURNAL, **48,** 2385 (1926).

[4] Hiers and Adams, *Ber.*, **59,** 162 (1926).

[5] Wallach, *Ann.*, **353,** 297 (1907).

The solution was cooled, made alkaline, and ether extracted. The base was dried and distilled and converted to the hydrochloride; hydrochloride salt, m. p. 245–246°.

Cyclohexyldiethylamine was prepared by the method of Sabatier and Senderens:[6] b. p. 56–57° at 5 mm.; n_D^{25} 1.4560; d_{25}^{25} 0.8445; hydrochloride from benzene and petroleum ether, m. p. 152–153°.

General Method of Preparation of Amines and their Salts.—About 20 g. of bromide was mixed with three molecular equivalents of dialkyl amine and allowed to stand at room temperature. Crystals of hydrobromide separated. About 100 cc. of water was added and the solution, after acidification with hydrochloric acid, was ether extracted to remove unreacted bromide, then made alkaline and again ether extracted to remove the product. The base was dried with solid potassium hydroxide, then with metallic sodium and fractionated.

The hydrochlorides were prepared by dissolving the amines in dry ether, precipitating by passing in dry hydrogen chloride and recrystallizing the crude products from a suitable solvent. Excess of hydrogen chloride should be avoided; otherwise the hydrochlorides may separate as oils. These oils may be converted into crystalline products by evaporating the solvent, adding chloroform, re-evaporating, and recrystallizing with or without the addition of a second solvent such as petroleum ether.

TABLE II

ω-CYCLOHEXYLALKYL TERTIARY AMINES, $C_6H_{11}(CH_2)_xN(C_2H_5)_2$

X =	B. p., °C.	n_D^{25}	d_{25}^{25}	Time of standing in preparation, weeks
1	73–75 (3.5 mm.)	1.4551	0.8361	5
2	81–82 (3 mm.)	1.4582	.8421	4
3	95–98 (3 mm.)	1.4587	.8392	2
4	109–111 (3 mm.)	1.4613	.8414	2
5	124–126 (3 mm.)	1.4620	.8445	4

ω-Cyclohexylalkyl Tertiary Amine Hydrochlorides, $C_6H_{11}(CH_2)_xN(C_2H_5)_2 \cdot HCl$

X =	M. p., °C.	Solvent for recrystallization	Calculated for	Chlorine, % Calcd.	Found
1	168–168.5	Benzene and ether	$C_{11}H_{23}N \cdot HCl$	17.28	17.30
2	155–156	$CHCl_3$ and CCl_4	$C_{12}H_{25}N \cdot HCl$	16.18	16.19
3	123–124	CCl_4 and pet. ether	$C_{13}H_{27}N \cdot HCl$	15.20	15.06
4	132–133	Abs. alc. and ether	$C_{14}H_{29}N \cdot HCl$	14.34	14.35
5	133–134	Abs. alc. and ether	$C_{15}H_{31}N \cdot HCl$	13.58	13.58
6	128–129	Abs. alc. and ether	$C_{16}H_{33}N \cdot HCl$	...	...

TABLE III

ω-CYCLOHEXYLALKYL TERTIARY AMINES, $C_6H_{11}(CH_2)_xNR_2$

X =	R =	B. p., °C.	n_D^{25}	d_{25}^{25}	Time of standing in preparation
4	n-C_3H_7	119–121 (2 mm.)	1.4598	0.8427	4 days
4	n-C_4H_9	135–138 (1.5 mm.)	1.4617	.8441	4 days
5	n-C_3H_7	143–144 (2.5 mm.)	1.4628	.8489	4 weeks

ω-Cyclohexylalkyl Tertiary Amine Hydrochlorides, $C_6H_{11}(CH_2)_xNR_2 \cdot HCl$

X =	R =	M. p., °C.	Solvent for recrystallization	Calcd. for	Chlorine, % Calcd.	Found
4	n-C_3H_7	120–121	Abs. alc. and ether	$C_{16}H_{33}N \cdot HCl$	12.89	13.02
4	n-C_4H_9	91–91.5	Abs. alc. and ether	$C_{18}H_{37}N \cdot HCl$	11.70	11.76
5	n-C_3H_7	103–104	Abs. alc. and ether	$C_{17}H_{35}N \cdot HCl$	12.27	12.30

[6] Sabatier and Senderens, *Compt. rend.*, **138**, 1258 (1904).

Summary

It has been shown that ω-cyclohexylalkyl amines of the general formula $C_6H_{11}(CH_2)_xNR_2$ are bactericidal to *B. leprae* providing the molecules have the proper molecular weight. The compounds should contain fifteen to eighteen carbon atoms just as found necessary in the various acids already tested, distribution of the carbon atoms having very little effect.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NORTH CAROLINA AND SYRACUSE UNIVERSITY]

THE IDENTIFICATION OF MERCAPTANS WITH 2,4-DINITROCHLOROBENZENE

BY R. W. BOST, J. O. TURNER AND R. D. NORTON

RECEIVED DECEMBER 21, 1931 PUBLISHED MAY 7, 1932

Due to the increasing interest shown in mercaptans and due to the paucity of good reagents whereby they may be identified, it seemed desirable to study methods for their identification. Numerous mercaptides[1,2,3] have been prepared. Purification of these is not always easy and certain of the mercaptides are frequently unstable.[4] Wertheim[1] has proposed 3,5-dinitrobenzoyl chloride and also 3-nitrophthalic anhydride as reagents for mercaptan identification. The use of these reagents is restricted, due to the close proximity of the melting points of certain of their derivatives. Reid[5] and his co-workers have suggested the use of sodium anthraquinone α-sulfonate and also sodium anthraquinone 1,5- and 1,8- disulfonates, although the sulfonic group could not be replaced with phenyl mercaptan. The time required for these reactions to go to completion varies from a few minutes to several hours, while in certain cases several products are obtained.

In this paper the authors propose 2,4-dinitrochlorobenzene as a new reagent for the identification of mercaptans. It rapidly forms solids with all mercaptans thus far studied. The reagent is inexpensive, it is stable, and gives excellent yields of stable derivatives which are easily purified, having sharp melting points and definite crystalline structure. In no case was it necessary to heat the reactants for over ten minutes. The reagent is unique in that it forms solid sulfides that can be rapidly oxidized to the corresponding sulfones, thus ensuring complete identification in a remarkably short time.

[1] Wertheim, THIS JOURNAL, **51**, 3661 (1929).

[2] Bennett, *J. Chem. Soc.*, **121**, 2139 (1922).

[3] Schacht, *Ann.*, **129**, 1 (1864).

[4] Borgstrom, Ellis and Reid, THIS JOURNAL, **51**, 3649 (1929).

[5] Reid, Mackall and Miller, *ibid.*, **43**, 2108 (1921).