Summary

On heating sodium or potassium methide, methane is evolved in accordance with the equation $4MCH_3 \longrightarrow 3CH_4 + M_4C$. Hydrolysis of the residue yields chiefly acetylene and hydrogen, together with some ethylene and ethane, indicating the transformation $2M_4C \longrightarrow M_2C_2 + 6M$. The thermolysis of sodium methide becomes rapid at about 200° and may be completed at a slightly higher temperature. The thermolysis of potassium methide first becomes rapid at 100° but is not completed below 250°. In this behavior evidence is found for the intervention of K_2CH_2 or K_3CH in the passage from KCH_3 to K_4C. The mechanisms of these reactions are discussed.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF ILLINOIS]

CYCLOBUTYLALKYL ALKYL ACETIC ACIDS AND THEIR BACTERICIDAL ACTION TOWARD B. LEPRAE. XVI[1]

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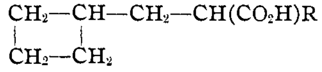
In a number of previous papers in this series[2] it was shown that certain ω-cyclohexylalkyl, ω-cyclopentylalkyl, ω-cyclopentenylalkyl and ω-cyclopropylalkyl alkyl acetic acids were bactericidal toward *B. Leprae*. The preparation of various cyclobutylmethyl alkyl acetic acids (I) was undertaken at the same time, but owing to experimental difficulties the compounds were not completed before the interesting discovery was made that no ring structure in the molecule was necessary for bactericidal action. The research on the cyclobutyl derivatives, however, was continued and results are described in this communication. Cyclobutylmethyl alkyl acetic acids (I) were prepared in which the alkyl group was *n*-octyl, *n*-nonyl, *n*-decyl, *n*-undecyl and *n*-dodecyl.

(I)



The bacteriological tests have shown that molecular weight is an important factor, as might have been anticipated from the study of the previous compounds which were prepared and tested. Those molecules which contained sixteen to eighteen carbon atoms were the most effective and gave results comparable to the other ring acids of the same molecular weight.

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[1] This communication is an abstract of a portion of a thesis submitted by S. G. Ford in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Illinois.

[2] For previous articles, see paper XV of this series, Stanley, Jay and Adams, THIS JOURNAL, **51**, 1261 (1929).

TABLE I

BACTERIOLOGICAL ACTION OF CYCLOBUTYL ALKYL ACETIC ACIDS TO *B. Leprae*

	Dilutions of sodium salts in thousands											
	5	25	50	62	74	85	100	125	155	192	250	333
$C_4H_7CH_2CH(CO_2H)C_8H_{17}$-*n*	−	−	−	−	−	±	+	+	+	+	+	+
$C_4H_7CH_2CH(CO_2H)C_9H_{19}$-*n*	−	−	−	−	−	−	−	±	±	+	+	+
$C_4H_7CH_2CH(CO_2H)C_{10}H_{21}$-*n*	−	−	−	−	−	−	−	−	±	±	+	+
$C_4H_7CH_2CH(CO_2H)C_{11}H_{23}$-*n*	−	−	−	−	−	±	±	±	+	+	+	+
$C_4H_7CH_2CH(CO_2H)C_{12}H_{25}$-*n*	−	−	+	+	+	+	+	+	+	+	+	+

The cyclobutylmethyl alkyl acetic acids were prepared through the malonic ester synthesis, by the use of cyclobutylmethyl bromide and the necessary diethyl monoalkyl malonates.

The diethyl ester of cyclobutane-1,1-dicarboxylic acid was prepared[3] and by direct reduction converted to cyclobutyl carbinol. Care had to be taken in conversion of the alcohol to the corresponding bromide. Demjanow[4] has shown that cyclobutyl carbinol when treated with hydrobromic acid rearranges to cyclopentyl bromide. A method which proved most successful for forming the bromide without rearrangement was a modification of that of Darzens,[5] in which the alcohol was treated with phosphorus tribromide in the presence of pyridine. By this procedure all free acid was avoided and the reaction ran smoothly, though with poor yields, to give cyclobutylmethyl bromide.

The authors are indebted to Dr. W. M. Stanley for carrying out the bacteriological tests.

Experimental

1,1-Dicarbo-ethoxycyclobutane.—The method of Kishner[3] was followed with success. The yield was 38% of a product boiling at 110–113° (20 mm.); n_D^{25} 1.4373; d_4^{25} 1.0445.

Cyclobutyl Carbinol.—A total of 365 g. of tetramethylene dicarboxylic ester was reduced to cyclobutyl carbinol in seven separate reductions by the toluene method.[6] In each experiment 52 g. of tetramethylene dicarboxylic ester, 650 cc. of absolute alcohol, 85 g. of sodium and 200 cc. of anhydrous toluene were used. After each reduction the excess ethyl alcohol was distilled off under slightly diminished pressure, two or three reduction mixtures combined, placed in a continuous extractor and extracted with ether for thirty-six hours. The ether was evaporated and the cyclobutyl carbinol distilled at atmospheric pressure. The yield was 76 g. (48.5%) of a product boiling at 140–143°; n_D^{25} 1.4449.

Cyclobutylmethyl Bromide.[7]—This was made by a modification of the method of

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[3] (a) Kishner, *J. Russ. Phys.-Chem. Soc.*, **37**, 507 (1905); (b) Zelinsky, *Ber.*, **46**, 1093 (1913); (c) *ibid.*, **60**, 711 (1927).

[4] Demjanow, *Ber.*, **40**, 4959 (1907); *J. Russ. Phys.-Chem. Soc.*, **35**, 26 (1903); *ibid.*, **42**, 837 (1910).

[5] Darzens, *Compt. rend.*, **152**, 1314 (1911).

[6] Stanley and Adams, THIS JOURNAL, **51**, 1515 (1929).

[7] V. Braun, Fussgänger and Kuhn, *Ann.*, **445**, 201 (1925), first prepared this substance by the action of phosphorus pentabromide on benzoyl cyclobutylmethyl amide.

Darzens.[5] A mixture of 59 g. of cyclobutyl carbinol, 17.5 g. of anhydrous pyridine and 50 cc. of dry ether was placed in a 200-cc., three-necked flask equipped with a stirrer, dropping funnel and a loosely-stoppered thermometer. The flask was immersed in an ice–salt bath and when the temperature of the contents of the flask had dropped to −10°, there was added with stirring a previously cooled solution of 62 g. of phosphorus tribromide in 30 cc. of absolute ether sufficiently slowly to keep the reaction mixture below −5°. After standing at 0° for two hours, the liquid was decanted from the solid material. The solid material was washed with cold anhydrous petroleum ether (25–40°) and the ether combined with the decanted liquid. The cold solution was neutralized with cold 50% potassium hydroxide solution, washed with water and the ethereal solution dried over anhydrous potassium carbonate. The ether was removed and the cyclobutylmethyl bromide was distilled under reduced pressure. The yield was 25 g. (29%) of a product boiling at 54–56° (45 mm.); n_D^{20} 1.4768.

Diethyl Cyclobutylmethyl Alkyl Malonates.—These were prepared by a method previously described,[8] by the condensation of cyclobutylmethyl bromide with diethyl mono-alkyl malonates.

TABLE II

DIETHYL CYCLOBUTYLMETHYL ALKYL MALONATES: $C_4H_7CH_2CH(CO_2H)R$

R =	B. p., °C.	n_D^{25}	d_4^{25}	Calculated, %		Found, %	
				C	H	C	H
n-C_8H_{17}	160–163 (3 mm.)	1.4558	0.9558	70.52	10.67	70.11	10.65
n-C_9H_{19}	168–171 (2.8 mm.)	1.4569	.9552	71.12	10.81	70.82	10.84
n-$C_{10}H_{21}$	177–181 (3 mm.)	1.4578	.9466	71.68	10.95	71.30	10.94
n-$C_{11}H_{23}$	188–191 (3.2 mm.)	1.4582	.9458	72.19	11.08	71.69	11.05
n-$C_{12}H_{25}$	196–199 (3 mm.)	1.4590	.9393	72.66	11.19	72.59	11.23

Cyclobutylmethyl Alkyl Acetic Acids.—These were prepared from the malonic acids by a method previously described.[4]

TABLE III

CYCLOBUTYLMETHYL ALKYL ACETIC ACIDS: $C_4H_7CH_2CH(CO_2H)R$

R =	B. p., °C.	n_D^{25}	d_4^{25}	Calculated, %		Found, %	
				C	H	C	H
n-C_8H_{17}	150–152 (2 mm.)	1.4615	0.9154	74.94	11.74	74.31	11.78
n-C_9H_{19}	177–181 (3.5 mm.)	1.4622	.9124	75.53	11.90	75.06	11.84
n-$C_{10}H_{21}$	176–179 (2.7 mm.)	1.4628	.9095	76.05	12.02	75.93	11.95
n-$C_{11}H_{23}$	188–192 (2.5 mm.)	1.4635	.9080	76.52	12.14	76.05	12.08
n-$C_{12}H_{25}$	204–205 (2.5 mm.)	1.4642	.9046	76.95	12.26	76.72	12.20

Summary

A series of cyclobutylmethyl alkyl acetic acids has been prepared and tested for bactericidal action to acid-fast bacteria.

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[8] Adams, Stanley and Stearns, THIS JOURNAL, 50, 1475 (1928).