compounds in the form of their sodium salts were much more effective than the sodium salts of pure chaulmoogric or hydnocarpic acids or the sodium salts of any of the mixed acids from natural oils containing chaulmoogric or hydnocarpic acids.

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

# CERTAIN $\Delta^2$ -CYCLOPENTENYL ALKYL ACETIC ACIDS AND THEIR ACTION TOWARD B. LEPRAE. IX<sup>1</sup>

By James A. Arvin<sup>2</sup> with Roger Adams Received August 29, 1927 Published November 5, 1927

The effect of the size of the side chain on the bactericidal character of various acids containing the cyclohexyl group was shown in a research described in the preceding paper.<sup>1</sup> The number of carbon atoms present apparently played such an important role in these compounds that it seemed probable that it would play just as important a one certainly in other series of acids, and probably in other classes of compounds now being studied in this same field.

Perkins<sup>3</sup> prepared  $\Delta^2$ -cyclopentenyl alkyl acetic acids in which the alkyl group was ethyl, *n*-propyl, *n*-butyl and allyl, and reported that some of these acids showed sufficient bactericidal action toward *B. Leprae* to warrant clinical testing. Judging from the results on cyclic acids in this Laboratory, by far the most effective compounds in this series should be those in which the alkyl group is octyl, or nonyl, or of even higher molecular weight. Since these substances have not previously been made, a series of  $\Delta^2$ -cyclopentenyl alkyl acetic acids has been produced and tested in which the alkyl group varies from *n*-amyl to *n*-nonyl (I).



The results were exactly those predicted. The bactericidal action increased very rapidly from *n*-amyl to the *n*-nonyl, the *n*-hexyl killing in dilutions of 1:10,000, but the higher molecular weight compounds in very much greater dilutions, 1:150,000 in the *n*-nonyl (Table I).

The compounds were prepared by condensing the sodium derivative of diethyl- $\Delta^2$ -cyclopentenyl malonate with various alkyl halides, preferably in the absence of the alcohol, so that a higher temperature might be reached

<sup>1</sup> Paper VIII in this series, THIS JOURNAL, **49**, 2934 (1927).

<sup>2</sup> This communication is an abstract of a portion of the thesis submitted by James A. Arvin in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

<sup>3</sup> Perkins and Cruz, THIS JOURNAL, 49, 517 (1927).

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		Dilutions of sodium salts																									
	1000	2000	5000	10,000	20,000	30,000	40,000	50,000	60,000	70,000	80,000	90'00	100,000	110,000	120,000	130,000	140,000	150,000	160,000	170,000	180,000	190,000	200,000	220,000	240,000	260,000	280,000 300,000
					$\Delta^2$ .	Cyc	lop	ent	eny	'l al	kyl	ace	etic	acio	ds,	C₅H	[7C]	H(R	.)C(	O2H		R ≃					
n-C5H11			÷		+	+	+	+	+	+	+	+															
n-C6H13					*	+	+	+	+	+	+	+															
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and a better yield of product formed. The di-substituted malonic esters were then saponified with alcoholic potash in the usual way and the dibasic acids converted to the monobasic acids merely by heating above the melting point.

The bacteriological work was carried out by Gerald H. Coleman and W. M. Stanley.

## Experimental

Diethyl- $\Delta^2$ -cyclopentenyl Malonate.—The procedure for obtaining this ester was a slight modification of that used by Noller and Adams.<sup>4</sup> Instead of an excess of dry hydrogen chloride, the gas was passed into the redistilled cyclopentadiene until 1 molecular equivalent had been absorbed. The reaction mixture was allowed to stand for two hours at  $-5^\circ$  to  $-10^\circ$ , and then without distillation was added to 1.25 molecular equivalents of sodium malonic ester in absolute alcohol. The conditions of condensation were described in a previous paper.<sup>4</sup> The ester was isolated in the usual way. The yield of the product boiling at 113–118° under 5 mm. was 80–85% of the theoretical.

Diethyl- $\Delta^2$ -cyclopentenyl Alkyl Malonate.—After preparing the sodium derivative of diethyl- $\Delta$ -cyclopentenyl malonate in the usual way from 5.8 g. of sodium, 175 cc. of absolute alcohol and 56.5 g. of diethyl- $\Delta^2$ -cyclopentenyl malonate, 135 cc. of alcohol was distilled off from the mixture. The alkyl bromide (0.3 mole) was then added and refluxing was continued for forty-eight hours. The rest of the alcohol was then distilled and water added to dissolve the sodium bromide. The products were then isolated in the usual way. The yields of the di-substituted esters from *n*-amyl to *n*-nonyl inclusive were, respectively, 37, 39, 35, 34 and 42% of the calculated amount. There was always recovered from 45-50% of pure diethyl- $\Delta^2$ -cyclopentenyl malonate unchanged.

TABLE II

#### $C_{\delta}H_7C(CO_2C_2H_{\delta})_2R$ , Diethyl- $\Delta^2$ -Cyclopentenyl Alkyl Malonates

		an 20	J20	Carbo	on, %	Hydrogen, %		
R =	В. р., °С.	"р	u 4	Calcd.	Found	Calcd.	Found	
$n-C_{b}H_{11}$	133–136 (3 mm.)	1.4580	0.9981	68.94	69.01	9.48	9.83	
$n-C_6H_{18}$	150–155 (4 mm.)	1.4572	.9867	69.60	69.89	9.75	10.06	
$n-C_7H_{15}$	159–164 (3 mm.)	1.4582	.9791	70.32	70.89	9.94	9.94	
$n - C_8 H_{17}$	169–174 (4 mm.)	1.4591	.9765	70.93	70.63	10.12	10.31	
$n-C_{9}H_{19}$	183–187 (5 mm.)	1.4595	.9756	71.53	71.81	10.29	10.53	

 $\Delta^2$ -Cyclopentenyl Alkyl Acetic Acids.—A solution of 17 g. of potassium hydroxide in 75 cc. of alcohol was refluxed on a steam-bath with 0.1 mole of pure diethyl- $\Delta^2$ cyclopentenyl alkyl malonate for twenty-four hours. The reaction mixture was then

\* Noller with Adams, THIS JOURNAL, 48, 1080 (1926).

diluted with 60 cc. of water and distilled until the temperature of the mixture reached about 98°. The residue was refluxed for two hours. It was then cooled to 10° and acidified with coned. hydrochloric acid, using Congo Red paper as an indicator. The malonic acid was separated and the aqueous liquors were extracted with ether. The separated malonic acid was also dissolved in the ether, the ether solutions mixed and dried with calcium chloride and then the ether evaporated. The residue was heated in a round-bottomed flask with an air-cooled reflux condenser for two hours at  $160-165^\circ$ . The residue was distilled under diminished pressure and the yields of the five monobasic acids from *n*-amyl to *n*-nonyl were, respectively, 70, 51, 55, 61 and 72% of the calculated amount.

#### TABLE III

#### $\Delta^2$ -Cyclopentenyl Alkyl Acetic Acids

B n °C	$n_{-}^{20}$	d <sup>20</sup>	Carbo	n, %	Hydro	gen, %
в.р., С.	D	-	Calcu,	round	Calcu.	Found
142–145 (5 mm.)	1.4659	0.9629	73.39	73.41	10.27	10.59
150-155 (5 mm.)	1.4671	.9573	74.21	73.88	10.56	10.73
162-165 (4 mm.)	1.4683	.9499	74.93	75.18	10.78	11.05
170-173 (4 mm.)	1.4687	.9452	75.58	76.19	10.99	11.43
173–176 (3 mm.)	1.4690	.9436	75.80	76.10	11.13	11.12
	B. p., °C. 142–145 (5 mm.) 150–155 (5 mm.) 162–165 (4 mm.) 170–173 (4 mm.) 173–176 (3 mm.)	B. p., °C. $n_D^{20}$ 142–145 (5 mm.) 1.4659 150–155 (5 mm.) 1.4671 162–165 (4 mm.) 1.4683 170–173 (4 mm.) 1.4687 173–176 (3 mm.) 1.4690	$\begin{array}{cccccc} & & & & & & & & & & & & \\ & & & & & & $	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	B. p., °C. $n_D^{20}$ $d_4^{20}$ Carbon, % Calcd. Found           142-145 (5 mm.)         1.4659         0.9629         73.39         73.41           150-155 (5 mm.)         1.4671         .9573         74.21         73.88           162-165 (4 mm.)         1.4683         .9499         74.93         75.18           170-173 (4 mm.)         1.4687         .9452         75.58         76.19           173-176 (3 mm.)         1.4690         .9436         75.80         76.10	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$

### Summary

1.  $\Delta^2$ -Cyclopentenyl alkyl acetic acids where the alkyl varies from *n*-amyl to *n*-nonyl have been prepared.

2. The bactericidal action toward *B. Leprae* has been shown to increase rapidly with increase in molecular weight of the alkyl group.

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# STUDIES IN URETHANS. IV. ACYL DI-URETHANS AND THEIR REACTIONS WITH AMMONIA AND AMINES<sup>1</sup>

By S. BASTERFIELD, ESLI L. WOODS AND MYRON S. WHELEN Received September 13, 1927 Published November 5, 1927

In a study of guanidine derivatives, Nencki<sup>2</sup> observed that dicarbethoxyguanidine was decomposed by alcoholic ammonia at  $100^{\circ}$  into monocarbethoxyguanidine and urethan. Malonyldi-urethan was found by Conrad and Schulze<sup>3</sup> to be decomposed by the same reagent into malonamide, ammonium barbiturate and urethan. In neither of these reactions was a urethan grouping converted into a urea as might have been expected. The products obtained by Conrad and Schulze show that from some molecules of diurethan both urethan groups were removed, while from others only one was removed, and the carbethoxymalonamide so formed then condensed to barbituric acid.

The action of ammonia and amines on carbonyldi-urethan has been

<sup>1</sup> A preliminary version of this paper was received July 19, 1926.

<sup>2</sup> Nencki, Ber., 7, 1588 (1874).

<sup>3</sup> Conrad and Schulze, Ber., 42, 729 (1909).