

12.20. Found:³ C, 63.93, 64.07; H, 4.22, 4.30; S, 12.20, 12.17.

Oxidation of the sulfide with 30% hydrogen peroxide (Superoxol) in acetic acid-acetic anhydride gave *p*-chloro-phenyl phenacyl sulfone, m. p. 133-134° (previously pre-

(3) Microanalyses by Dr. Carl Tiedcke, New York, N. Y.

pared by a different method, m. p. 132-133°).⁴

(4) Tröger and Beck, *J. prakt. Chem.*, [2] **87**, 296 (1913).

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COMMUNICATIONS TO THE EDITOR

GROWTH INHIBITION OF LACTIC ACID BACTERIA BY N-(α,γ -DIHYDROXY- β,β -DIMETHYLVALERYL)- β -ALANINE AND ITS REVERSAL BY PANTOTHENIC ACID¹

Sir:

It has been observed that pantothenic acid molecules with modified non-nitrogenous moieties exhibited diminished or inappreciable growth activity.^{1a-3} Salicyl- β -alanine and mandelyl- β -alanine have been reported to be effective displacers of pantothenic acid.⁴ A few analogs possessed inhibitory properties but their effects were not reversed by pantothenic acid.³ In the present studies, the growth of lactic acid bacteria was inhibited markedly by N-(α,γ -dihydroxy- β,β -dimethylvaleryl)- β -alanine and the inhibition was reversed, competitively, by pantothenic acid over a wide range of concentrations.

α,α -Dimethyl- β -hydroxybutyraldehyde (b. p. 74-77° (15 mm.)), prepared as described by Lilienfeld and Tauss,⁵ was converted to α -hydroxy- β,β -dimethyl- γ -valerolactone (b. p. 93-94.5° (1 mm.)) by the method of Stiller, *et al.*⁶ The lactone crystallized from diethyl ether-petroleum ether as white hygroscopic needles. *Anal.* Calcd. for C₇H₁₂O₃: C, 58.31; H, 8.39. Found: C, 57.69; H, 8.47. The sodium salt of dl - N - (α,γ - dihydroxy - β,β - dimethylvaleryl) - β -alanine was prepared by fusing a mixture of the lactone and the sodium salt of β -alanine at 110-120°.

Acid production (ml. of 0.0385 N base to titrate final 3-ml. volumes) is shown in the Table I.

Mixtures of the lactone and β -alanine had little effect in concentrations as high as 10,000 γ per tube. It is of interest that stimulations occurred at low levels of the analog in the presence of pantothenic acid. Phenyl pantothenone has been reported to be stimulatory at sub-inhibitory levels.⁷

(1) Aided by grants from the National Institute of Health of the U. S. Public Health Service and the U. of California.

(1a) Williams, *Adv. in Enzym.*, **3**, 253 (1943).

(2) Nease, Dissertation, U. of Texas (1943); quoted by Snell and Shive, *J. Biol. Chem.*, **158**, 551 (1945).

(3) Mellwain, *Biochem. J.*, **36**, 417 (1942).

(4) Martin, Lewis and Urist, Abstracts of Papers, 109th Meeting, Am. Chem. Soc., 21B (1946).

(5) Lilienfeld and Tauss, *Monatsh.*, **19**, 77 (1898).

(6) Stiller, Harris, Finkelstein, Keresztesy and Folkers, *This Journal*, **62**, 1785 (1940).

(7) Woolley and Collyer, *J. Biol. Chem.*, **159**, 263 (1945).

TABLE I

Ca d-pantothenate per tube, γ	Analog ^a per tube, γ	<i>Lacto-bacillus arabinosus</i> 17-5, ml.	<i>Lacto-bacillus casei</i> 6, ml.	<i>Lacto-bacillus fermenti</i> 38, ml.	<i>Leuconostoc mesenteroides</i> P-60, ml.
0.0	0.0	4.05	1.80	1.55	2.33
.02	.0	9.95	4.78	2.10	4.50
.06	.0	13.90	10.45	3.70	6.90
.20	.0	14.85	14.18	6.00	9.00
.60	.0	14.90	15.57	8.30	10.65
.02	2.0	9.82	4.15	2.50	5.00
.02	6.0	9.45	2.05	2.55	5.15
.02	10.0	9.05	1.73	2.35	5.00
.02	20.0	8.05		2.28	4.00
.02	40	6.25		1.55	2.75
.02	80	4.05			2.30
.20	60	15.40	4.70	6.30	9.07
.20	100	14.75	2.15	5.70	8.35
.20	200	12.35	1.78	4.05	7.65
.20	400	8.90		1.62	6.50
.20	1000	4.05			2.30

Antibacterial

index³ 4000-5000 500-1000 2000 4000-5000

^a The analog was 83% condensed according to Van Slyke amino nitrogen determination.

Preliminary experiments with streptococci indicated a high *in vitro* susceptibility to the inhibitor. Further studies on the activity and toxicity of this and other analogs are in progress.

The Dissertation (U. of Texas, 1943) of A. H. Nease has come to our attention. It was reported that N-(α,γ -dihydroxy)- β,β -dimethylvaleryl)- β -alanine, prepared under the direction of Dr. H. R. Henze, had no growth activity for *L. casei*.

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THE RAMAN SPECTRUM OF CYCLOÖCTA-TETRAENE

Sir:

A material obtained from Germany through the courtesy of the Office of Research and Inventions, U. S. Navy, and Division 16, NDRC, purporting to be 1,3,5,7-cycloöctatetraene, has been found to boil at 142° (uncor.) in agreement with the litera-