TABLE II

GROWTH-PROMOTING ACTIVITIES OF HYDROGENATED COMPOUNDS

		Transmission, %		
	μg./10 ml.	Hydrogenated N^{10}-methyl PGA	Hydrogenated aminopterin	Hydrogenated A-methopterin
For *S. faecalis* R.	0.1	100	53	100
	1.0	100	36	100
	10.0	68	25	100
	100.0	66	26	100
For *L. citrovorum 8081*	0.1	90	91	91
	1.0	92	90	93
	10.0	90	77	94
	100.0	78	33	90

The hydrogenated materials were also tested as growth factors for *Streptococcus faecalis* R. and *Leuconostoc citrovorum 8081*. For the former organism, the same basal medium was used as was used for the inhibition studies but no folic acid was added. For the latter organism, the basal medium and technique of Sauberlich[8] were used with the exceptions that no supplementary glycine and alanine were used and a Lumitron colorimeter with a 660 mμ filter was employed. Turbidity was determined after 17 hours. Data are given in Table II. It is quite likely that the growth-promoting activity is due to an impurity in the original compound as suggested by Weygand.

Acknowledgment.—The authors wish to thank Lederle Laboratories for supplying the folic acid, N^{10}-methylpteroylglutamic acid, aminopterin and A-methopterin used in these experiments.

(8) H. E. Sauberlich, *J. Biol. Chem.*, **181**, 467 (1949).

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COMMUNICATIONS TO THE EDITOR

A NEW METHOD FOR THE PREPARATION OF THIO ACIDS AND APPLICATION TO PEPTIDE CHEMISTRY

Sir:

Although Pawlewski[1] demonstrated that thio acids were very active acylating agents, the methods of preparation which have been available heretofore[2] have not been suitable for making the acylaminothio acids which could be useful in peptide synthesis. By passing hydrogen sulfide into a solution of the mixed anhydrides,[3,4,5] RCOO-$COOC_2H_6$, in methylene chloride with an equivalent of triethylamine at −20° and warming to room temperature, we have obtained the thio acids, RCOSH.

In this manner we have prepared, in addition to thioacetic and thiobenzoic acids, *p*-phenylthiobenzoic acid, 88% yield (from the carboxylic acid), m.p. 90–92° (*Anal.* Calcd. for $C_{13}H_{10}OS$: C, 72.89; H, 4.71; S, 14.94. Found: C, 72.86; H, 4.83; S, 15.09); thiohippuric acid, 70% yield, m.p. 98–100° (*Anal.* Calcd. for $C_9H_9NO_2S$: C, 55.39; H, 4.65; N, 7.18; S, 16.40. Found: C, 55.30; H, 4.69; N, 6.79; S, 15.99); phthaloylthioglycine, 45% yield, m.p. 114–116° (*Anal.* Calcd. for $C_{10}H_7NO_3S$: C, 54.30; H, 3.19; S, 14.47. Found: C, 54.52; H, 3.32; S, 14.21).

When thiohippuric acid was warmed to 90–110° in dimethylformamide with *d,l*-alanine in a nitrogen atmosphere, hydrogen sulfide was rapidly evolved and there was obtained a 70% yield of hippuryl-alanine, m.p. 200–201.5°[6] and giving the correct elemental analysis.

Upon treatment of thiohippuric acid with Raney nickel which had been deactivated over acetone[7] there was obtained in one experiment, a 30% yield of hippuraldehyde,[8] isolated as the 2,4-dinitrophenylhydrazone, m.p. 200–202° (*Anal.* Calcd. for $C_{15}H_{13}N_5O_5$: C, 52.48; H, 3.82; N, 20.40. Found: C, 52.63; H, 3.78; N, 20.18).

(1) Br. Pawlewski, *Ber.*, **31**, 661 (1898); **34**, 657 (1901); **35**, 110 (1902).

(2) R. Connor, "Organic Sulfur Compounds," p. 835 in Gilman's "Organic Chemistry," Vol. I, Second Edition, John Wiley and Sons, Inc., New York, N. Y., 1943; S. Sunner and T. Nilson, *Svensk. Kem. Tid.*, **54**, 163 (1942) [*C. A.*, **38**, 3249 (1944)]; B. Tchoubar and Letellier-Dupre, *Bull. soc. chim. France*, 792 (1947).

(3) R. A. Boissonnas, *Helv. Chim. Acta*, **34**, 874 (1951); T. Wieland and H. Bernhard, *Ann.*, **572**, 190 (1951); J. R. Vaughan and R. L. Osato, THIS JOURNAL, **74**, 676 (1952).

(4) T. Wieland, W. Schäfer and E. Bokelmann, *Ann.*, **573**, 99 (1951), prepared $RCOSC_6H_5$ by addition of C_6H_5SH to the mixed anhydride.

(5) H. Adkins and Q. E. Thompson, THIS JOURNAL, **71**, 2242 (1949), prepared thiobenzoic acid by passing H_2S into dibenzoyl sulfide in pyridine.

(6) T. Curtius and E. Lambotte, *J. prakt. Chem.*, [2] **70**, 114 (1904).

(7) G. B. Spero, A. V. McIntosh and R. H. Levin, THIS JOURNAL, **70**, 1907 (1948).

(8) J. Bougault, E. Cattelain and P. Chabrier, *Bull. soc. chim.*, [5] **5**, 1699 (1938), have reported the conversion of thioacetic acid to acetaldehyde.

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THE SYNTHESIS AND REACTIONS OF N-ACYL THIOL AMINO ACIDS

Sir:

Recent evidence that enzymatic acylations involve thiolacid derivatives as activated intermediates[1] has stimulated interest in similar thiol analogs of amino acids as possible participants in the physiological synthesis of peptides. By two

(1) For example, acetyl coenzyme A is considered to be a key intermediate in biological acetylations; F. Lynen, E. Reichert and L. Rueff, *Ann.*, **574**, 1 (1951); T. C. Chou and F. Lipmann, *J. Biol. Chem.*, **196**, 89 (1952).