TABLE I

EFFECT OF VARIOUS SUPPLEMENTS ON GROWTH OF *E. coli* ON COMPLETE MEDIUM PLUS 4-AMINO PGA

Addition per ml. basal medium[a]	Optical density after 16 hours at 37° Expt. 1	Expt. 2	Addition per ml. basal medium[a]	Optical density after 16 hours at 37° Expt. 1	Expt. 2
None	0.09	0.05	100 γ thymidine	..	0.32
3.0 c. mm. liver extract	.16	.20	10 γ guanine desoxyriboside	0.10	.06
10 c. mm. liver extract	.27	.28	100 γ guanine desoxyriboside	..	.09
100 c. mm. liver extract	..	.38	10 γ hypoxanthine desoxyriboside	.09	.06
3 γ thymine	.06	..	100 γ hypoxanthine desoxyriboside	..	.08
50 γ thymine	..	.08	0.01 γ vitamin B_{12}	.08	.07
0.1 γ thymidine	.14	.12	0.1 γ vitamin B_{12}	..	.10
1.0 γ thymidine	.24	.18	0.4 mg. pteroylglutamic acid	..	.08
10 γ thymidine	..	.26	0.5 mg. *p*-aminobenzoic acid	..	.06

[a] Landy–Dicken[b] medium with dextrose in place of sucrose *plus* 0.15 mg. (Expt. 1) or 0.25 mg. (Expt. 2) 4-amino PGA per ml. of culture medium. Final volume 2 ml. per tube. Inoculum: 24 hour culture on broth,[c] washed once and diluted 1:10. Reading with 4-amino PGA omitted, about 0.4. [b] Landy and Dicken, *J. Lab. Clin. Med.*, **27**, 1086 (1942). [c] Teply and Elvehjem, *J. Biol. Chem.*, **157**, 303 (1945).

with *Lactobacillus leichmannii* was similar to that of Snell and co-workers[2] but with thioglycolic acid, 0.2 mg. per ml.[7] When 25 γ of 4-amino PGA per ml. and 0.2 γ of PGA were added, the following are typical of optical densities obtained at 18 hours: no supplement, 0.02; 200 γ PGA, 0.04; 0.01 γ B_{12}, 0.05; 2 γ thymidine, 0.58; 2 γ guanine desoxyriboside, 0.08; 2 γ hypoxanthine desoxyriboside, 0.04; 100 γ thymine, 0.10; 100 γ thymine *plus* 2 mγ vitamin B_{12}, 0.29. The addition of 2 mγ of vitamin B_{12} did not augment the growth obtained with the desoxyribosides. When 4-amino PGA, PGA and *p*-aminobenzoic acid were omitted from the basal medium the following optical densities were obtained: no supplement, 0.03; 2 mγ B_{12}, 0.27; 2 γ guanine desoxyriboside, 0.37; 2 γ hypoxanthine desoxyriboside, 0.37; 2 γ thymidine, 0.52; 2 mγ B_{12} *plus* 0.2 γ PGA, 1.5; 2 γ guanine desoxyriboside *plus* 0.2 γ PGA, 1.1; 2 γ hypoxanthine desoxyriboside *plus* 0.2 γ PGA, 1.1; 2 γ thymidine *plus* 0.2 γ PGA, 1.2.

Discussion.—The inhibitory effects of low levels of 4-amino PGA for certain organisms are reversible by PGA but high levels of the antagonist produce toxic effects which are not so reverse.[8,9,10] The present investigation shows that these toxic effects may in certain instances be reversed by thymidine, which may indicate that PGA has a role in the formation of thymidine. The inhibitory effect of 4-amino PGA on the growth of *E. coli* conceivably may be due to the entrance of this substance into the cell to displace endogenously-formed PGA from this role. The inhibitory effect of "x-methyl-PGA" upon *Leuconostoc mesenteroides* 8293 was found by Shive and co-workers[11] to be reversed by either PGA or thymidine. After the present experiments were completed, Sauberlich[12] reported inhibition of the growth of *Leuconostoc citrovorum* 8081 by 4-amino PGA and reversal by thymidine. We are indebted to Dr. J. O. Lampen for thymidine, to Dr. H. M. Kalckar for guanine desoxyriboside and to Dr. E. E. Snell for hypoxanthine desoxyriboside.

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The Reduction of 2-Acetylpyridine to 2-Ethylpyridine

BY ARTHUR FURST

Recently Gregg and Craig[1] reported that the melting point of the picrate of 2-ethylpyridine made by two different methods—hydrogenation of 2-vinylpyridine and the action of methyl iodide on lithium picoline—did not agree with that obtained by Bergstrom and McAllister[2] who made it by the addition of ethylmagnesium bromide to pyridine. In confirmation of the work of the former authors 2-acetylpyridine was reduced to 2-ethylpyridine by three different methods, namely, Clemmensen, Wolff–Kishner, and Huang-Minlon. The results of the boiling points, melting points, mixed melting points, and fusion analysis[3] show that these reduction products agree in all respects with each other and with the compound obtained by Gregg and Craig by hydrogenation of 2-vinylpyridine.

Experimental

The 2-acetylpyridine, from Dougherty Chemical Co., was redistilled: picrate m. p. 131°; lit. 131°.[4]

Clemmensen Reduction.—A solution of 2-acetylpyridine (0.12 mole) in 70 ml. of concentrated hydrochloric acid was vigorously refluxed in contact with amalgamated zinc (0.77 mole).[5] After ten hours 50 ml. more acid was added, and refluxing was continued an additional five hours. The solution was made basic with solid hydroxide, filtered through a stainless steel funnel, extracted with benzene, dried and fractionated. The colorless distillate that came over at 144° was caught in a 50% alcoholic solution

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(2) F. W. Bergstrom and S. H. McAllister, *ibid.*, **52**, 2845 (1930).

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(4) H. Maier-Bode and J. Altpeter, "Das Pyridin und seine Derivative," Edwards Brothers, Inc., Ann Arbor, Mich., 1934, p. 197.

(5) E. L. Martin in "Organic Reactions," Vol. I, R. Adams, Ed. John Wiley and Sons, Inc., New York, N. Y., 1942, p. 163.

of picric acid. The solid was isolated as described below (yields).

Anal. Calcd. for $C_{13}H_{12}O_7N_4$: N, 16.7. Found: N, 16.7.

Wolff–Kishner.—A yield of 7.8 g. (83.5%) of the semicarbazide hydrochloride of 2-acetylpyridine was obtained by the method of Woodward, *et al.*,[6] using ten equivalents of hydrochloric acid, m. p. 202° (uncor.).

Anal. Calcd. for $C_8H_{10}ON_4 \cdot HCl$: N, 26.2; Cl, 16.6. Found: N, 26.6; Cl, 17.0, 16.9.

The reduction was carried out by heating the semicarbazide hydrochloride with eight equivalents of sodium ethylate in an oil-bath at 180°. The distillate was caught in a 50% alcoholic solution of picric acid.

Huang–Minlon.[7]—A mixture of 2-acetylpyridine (0.06 mole), 5 ml. of 85% hydrazine hydrate, 5 g. of sodium hydroxide, and 80 ml. of diethylene glycol was heated for six hours. No attempt was made to remove the water. The solution was cooled, extracted with benzene, and converted into the picrate.

Yields.—No attempt was made to obtain maximum yields. The solid picrates were isolated from the alcoholic solution, dissolved in hot acetone, treated with decolorizing carbon, crystallized by cooling and finally recrystallized from alcohol. From the weights of the crude products, and the purified picrates the following estimates of yields were made: Clemmensen 80%, Wolff–Kishner 50% and Huang-Minlon 65%.

Melting Points and Fusion Analysis.—Using a copper block[8] and raising the temperature at a rate no faster than 1–2° per minute each picrate, and all possible combinations of picrate mixtures melted at 107–107.5° (uncor.). When the picrate of the Clemmensen reduction product was mixed with (a) the picrate of 2-acetylpyridine a depression of 20° in the melting point was noted; (b) the picrate of the hydrogenation product of Gregg and Craig the melting point was 107.5°. A fusion analysis showed these last pair to be identical also, for no eutectic melt was noted at the boundary. This in contrast with the eutectic melt shown in the fusion analysis of the first pair.

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(6) C. F. Woodward, A. Eisner and P. G. Hains, THIS JOURNAL, **66**, 911 (1944).

(7) Huang-Minlon, *ibid.*, **68**, 2487 (1946).

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UNIVERSITY OF SAN FRANCISCO
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The Reaction of Propyl Disulfide with Decyl Mercaptan

BY GEORGE GORIN,[1] GREGG DOUGHERTY AND ARTHUR V. TOBOLSKY

It is known that thioglycolic acid reacts with cystine in solution to give cysteine[2]; indeed, a quantitative study of the reaction has been made.[3] We wish to report some results which indicate that a similar reaction occurs between simple alkyl disulfides and mercaptans.

Mixtures of propyl disulfide and decyl mercaptan were heated in sealed Pyrex glass tubes for varying lengths of time. The samples were then cooled, the mercaptans were titrated with standard silver nitrate solution to an amperometric end-point, and the precipitated silver mercaptides weighed.[4] It was found that the number of moles of total mercaptan did not change during the reaction, but that the weight of the precipitate decreased continuously to an equilibrium value. It was thus indicated that there had taken place a mole per mole exchange of propyl for decyl mercaptan. The data obtained in a run at 138–139° are given in Table I.

TABLE I

MIXTURES OF PROPYL DISULFIDE AND DECYL MERCAPTAN HEATED AT 138–139°

Time, hr.	Moles SH found	Av. mol. wt. of AgSR	% PrSH
0		280	1
3	275	268	13
6	282	260	21
9	276	253	29
12	278	248	34
36	277	243	39
62	277	226	56

At 180° the reaction proceeded more quickly, and after a few hours heating considerable amounts of propyl mercaptan could be isolated directly by distillation of the cooled reaction mixture.

We believe the reaction proceeds by a stepwise exchange which at first gives rise to a mixed disulfide. We made no attempt to isolate this compound but hope to obtain evidence on this question in future work.

Experimental

Material.—The propyl disulfide was an Eastman Kodak Co. "white label" product which had been redistilled at least once, b. p. 93.3–94.6° at 30 mm. The decyl mercaptan was a Connecticut Hard Rubber Co. product, which had been redistilled at least once; b. p. 102–106° at 15 mm., $n^{30}D$ 1.4534, molecular weight[4] 171 (calculated 174).

Approximate Rate Measurements.—Equal volumes (1.00 ml.) of a mixture of one mole of propyl disulfide and one mole decyl mercaptan were sealed in several tubes of nearly equal volumes (1.5 ml.) and heated in a vapor bath for some time (*p*-xylene used at 138–139°; *p*-cymene at 176°). At the end of the appropriate period each tube was withdrawn and cooled, and the contents washed into 375 ml. of 95% alcohol containing 25 ml. of 0.2 *M* alcoholic ammonium acetate as supporting electrolyte. The solution was then titrated with standard 0.1 *N* alcoholic silver nitrate to an amperometric end-point. The precipitate was transferred to Gooch-type filters consisting of a layer of asbestos placed over a medium Pyrex glass fritted filter disk, and dried *in vacuo* at 60–70° to constant weight.

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