rived from liquid sulfides or mixed melting points of the solid sulfides were taken in all cases.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF ROCHESTER
ROCHESTER, NEW YORK

RECEIVED MAY 22, 1951

The Synthesis of New β-Diketones

BY ROBERT LEVINE AND JAMES K. SNEED

For other work, which is now in progress in this Laboratory, the following four β-diketones were required.

Nicotinoyltrifluoroacetone.—Commercial sodium methoxide (0.2 mole, 11.4 g. of commercial 95% material[1]) was placed in a 1000-ml. three-neck, round-bottom flask, equipped with ground glass joints and carrying a mercury-sealed stirrer, a reflux condenser and dropping funnel (drying tubes). The sodium methoxide was suspended in 250 ml. of anhydrous ether and to the rapidly stirred mixture, cooled in an ice-bath, 0.2 mole (28.4 g.) of ethyl trifluoroacetate, diluted to 125 ml. with anhydrous ether, was added. The ice-bath was removed and then 0.2 mole (24.2 g.) of 3-acetylpyridine, diluted to 125 ml. with anhydrous ether, was added dropwise. After the addition of the ketone was complete, the mixture was stirred and refluxed for two hours on a water-bath. The water bath was removed and water (*ca.* 100 ml., exothermic reaction) was added slowly to dissolve the solid which was present and the mixture extracted with several 100-ml. portions of ether to remove unreacted ester and ketone. The aqueous phase was acidified with 0.2 mole of glacial acetic acid and extracted with ether until the extracts no longer gave a positive test with alcoholic iron(III) chloride solution. The combined extracts were dried over Drierite, the solvent distilled and the residue crystallized to give 38.2 g. (88.0%) of nicotinoyltrifluoroacetone, m.p. 173.5–174°. *Anal.* Calcd. for $C_9H_6O_2NF_3$: C, 49.78; H, 2.79. Found: C, 49.87; H, 2.86. The β-diketone gave a green copper chelate, m.p. 262–262.5°. *Anal.* Calcd. for $C_{18}H_{10}O_4N_2F_6Cu$: C, 43.60; H, 2.02. Found: C, 43.34; H, 1.91.

Isonicotinoyltrifluoroacetone.—Using the apparatus described above, a mixture of 0.345 mole (47.3 g.) of 4-acetylpyridine, 0.345 mole (19.6 g.) of 95% sodium methoxide and 0.345 mole (49.0 g.) of ethyl trifluoroacetate was refluxed for six hours. Then, the addition of 0.345 mole (20.5 g.) of glacial acetic acid caused the precipitation of a mixture of sodium acetate and condensation product. Water (*ca.* 250 ml.) was added to the vigorously stirred reaction mixture to dissolve the sodium acetate and the mixture filtered. The precipitate was washed with several portions of water and dried in a vacuum desiccator. In this manner, there was obtained 71.4 g. (95.2%) of isonicotinoyltrifluoroacetone, m.p. 213–214.5° (sealed tube). *Anal.* Calcd. for $C_9H_6O_2NF_3$: C, 49.78; H, 2.79. Found: C, 49.81; H, 2.75. The β-diketone gave a green copper chelate, which decomposed without melting when heated above 280°. *Anal.* Calcd. for $C_{18}H_{10}O_4N_2F_6Cu$: C, 43.60; H, 2.02. Found: C, 43.40; H, 1.77.

Nicotinoyl-2-thenoylmethane.—When 0.25 mole (31.5 g.) of 2-acetylthiophene, 0.3 mole (41.1 g.) of methyl nicotinate and 0.50 mole of sodium amide[2] (prepared from 11.5 g. of sodium) were allowed to react for two hours, as described previously for other heterocyclic β-diketones,[2] and the mixture worked up as described above for the preparation of nicotinoyltrifluoroacetone, there was obtained 34.1 g. (59%) of nicotinoyl-2-thenoylmethane, m.p. 133–134°. *Anal.* Calcd. for $C_{12}H_9O_2NS$: C, 62.32; H, 3.92. Found: C, 62.46; H, 3.68. The β-diketone formed a picrate, m.p. 208–209°. *Anal.* Calcd. for $C_{18}H_{12}O_9N_4S$: N, 12.17. Found: N, 12.29.

Isonicotinoyl-2-thenoylmethane.—A mixture of 0.50 mole (63.0 g.) of 2-acetylthiophene, 0.25 mole (34.3 g.) of methyl isonicotinate and 0.25 mole (14.5 g.) of 95% sodium methoxide was refluxed for six hours and the reaction stopped by the addition of glacial acetic acid and water as described above in the preparation of isonicotinoyltrifluoroacetone. The mixture was extracted with ether until a negative test was obtained with alcoholic iron(III) chloride solution, the extracts dried over Drierite and the solvent and unreacted reactants distilled. The residue was recrystallized from 95% ethanol to give 37.6 g. (64.8%) of isonicotinoyl-2-thenoylmethane; m.p. 152–152.5°. *Anal.* Calcd. for $C_{12}H_9O_2NS$: C, 62.32; H, 3.92. Found: C, 62.25; H, 3.68. The β-diketone gave a picrate, m.p. 211–212.5°. *Anal.* Calcd. for $C_{18}H_{12}O_9N_4S$: N, 12.17. Found: N, 12.42.

CONTRIBUTION NO. 818
DEPARTMENT OF CHEMISTRY
UNIVERSITY OF PITTSBURGH
PITTSBURGH 13, PENNSYLVANIA

RECEIVED APRIL 16, 1951

---

[1] Purchased from the Mathieson Chemical Corporation, Niagara Falls, N. Y.

[2] Harris and Levine, THIS JOURNAL, **70**, 3360 (1948).

Preparation and Microbiological Activity of an Homolog of Lysine

BY A. D. MCLAREN AND C. A. KNIGHT

Considerable attention has been directed recently to the investigation of compounds which are structurally similar to metabolically important substances.[1] In the present communication we are reporting the synthesis of a lysine homolog, ε-C-methyllysine (2,6-diaminoheptanoic acid), and some effects of this compound on the growth of 2 lactobacilli, *Leuconostoc mesenteroides* P-60 and *Streptococcus faecalis*, American Type Culture Collection No. 9790.

Experimental

The 2,6-diaminoheptanoic acid dihydrochloride was prepared by a several step synthesis according to the procedures of Eck and Marvel[2] from 2-methylcyclohexanone oxime.[3] The intermediates, 2-keto-7-methylhexamethylenimine and 6-aminoheptanoic acid, have been reported elsewhere.[3]

6-Benzoylaminoheptanoic Acid.—2-Methylcyclohexanone oxime, 630 g., was converted to the benzoylamino acid.[2] The product, m.p.[4] 87–89°, weighed 749 g.

Anal. Calcd. for $C_{14}H_{19}O_3N$: C, 67.42; H, 7.70. Found: C, 67.24; H, 7.70.

6-Benzoylamino-2-bromoheptanoic Acid.—6-Benzoylaminoheptanoic acid, 720 g., was brominated in the usual way.[2] The 2-bromo acid, m.p. 152–153.5°, crystallizes very slowly from acetone or chloroform over a period of months. Consequently some of the product was withdrawn and recrystallized for analyses and further syntheses.

Anal. Calcd. for $C_{14}H_{18}O_3NBr$: C, 51.23; H, 5.53; N, 4.27. Found: C, 51.57; H, 5.55; N, 4.51.

6-Benzoylamino-2-aminoheptanoic Acid.—The bromo-acid, 16 g., was allowed to react with ammonia according to the procedures of Eck and Marvel.[2] The product, m.p. 247–250°, weighed 9 g.

Anal. Calcd. for $C_{14}H_{20}O_3N_2$: C, 63.60; H, 7.62; N, 10.62. Found: C, 63.40; H, 7.72; N, 10.70.

2,6-Diaminoheptanoic Acid Dihydrochloride.—6-Benzoylamino-2-aminoheptanoic acid, 1 g., was hydrolyzed[2] to give 0.42 g. of ε-C-methyllysine dihydrochloride. The product, m.p. 190.5–192°, sinters at *ca.* 185° and releases bubbles at *ca.* 206°.

Anal. Calcd. for $C_7H_{18}O_2N_2Cl_2$: C, 36.02; H, 7.78; N, 12.02. Found: C, 36.21; H, 7.58; N, 11.89.

Tests for Lysine Activity and Lysine Inhibition.—Tests were set up for the microbiological assay of lysine using either *Streptococcus faecalis* or *Leuconostoc mesenteroides* and employing the conditions previously described[5] with the exceptions that the tests were run in a total volume of 2 ml.

---

[1] D. W. Woolley, *Physiol. Rev.*, **27**, 308 (1947).

[2] J. C. Eck and C. S. Marvel, "Organic Syntheses," Coll. Vol. 2, A. H. Blatt, Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 74, 76, 374.

[3] H. E. Ungnade and A. D. McLaren, *J. Org. Chem.*, **10**, 29 (1945).

[4] All melting points are corrected.

[5] C. A. Knight, *J. Biol. Chem.*, **171**, 297 (1947).