phenylhydrazide (II); m. p. 153.5–155.7° (cor.); $[\alpha]^{25}D$ 0.0° (3% in acetone). (I) was fractionally recrystallized from toluene to give 4.0 g. of N-carbobenzoxy-L-*o*-fluorophenylalanylphenyl-hydrazide (III); m. p. 171.0–172.0° (cor.); $[\alpha]^{25}D$ −31.0° (3% in acetone). *Anal.* Calcd. for $C_{23}H_{22}O_3N_3F$: C, 67.8; H, 5.4; N, 10.3. Found: C, 67.9; H, 5.7; N, 10.3; and 4.0 g. of (II); m. p. 155.5–156.5° (cor.); $[\alpha]^{25}D$ 0.0° (3% in acetone). *Anal.* Calcd. for $C_{23}H_{22}O_3N_3F$: C, 67.8; H, 5.4; N, 10.3. Found: C, 67.9; H, 5.6; N, 10.3. The filtrate from (II) was concentrated under reduced pressure, acidified, and the oily solid recrystallized from toluene to give 5.6 g. of an approximately equimolar mixture of N-carbobenzoxy-D-*o*-fluorophenylalanine and N-carbobenzoxy-DL-*o*-fluorophenylalanine. Fractional recrystallization from toluene gave 1.0 g. of N-carbobenzoxy-D-*o*-fluorophenylalanine (IV); m. p. 103–105° (cor.); $[\alpha]^{25}D$ +15.7° (5% in acetone). *Anal.* Calcd. for $C_{17}H_{16}O_4NF$: C, 64.3; H, 5.1; N, 4.4. Found: C, 64.4; H, 5.1; N, 4.2; and 1.9 g. of N-carbobenzoxy-DL-*o*-fluorophenylalanine (V); m. p. 108.5–110.0° (cor.); $[\alpha]^{25}D$ 0.2° (5% in acetone). *Anal.* Calcd. for $C_{17}H_{16}O_4NF$: C, 64.3; H, 5.1; N, 4.4. Found: C, 64.5; H, 5.3; N, 4.5.

A simultaneous enzymatic resolution of N-carbobenzoxy-DL-alanine using an aliquot of the same enzyme preparation gave N-carbobenzoxy-L-alanylphenylhydrazide in 75% yield after one recrystallization; m. p. 154.5–155.5° (cor.); $[\alpha]^{25}D$ −27.2° (5% in acetone).

Other experiments not reported here indicate that the behavior noted with *o*-fluorophenylalanine is not unique and it is clear that further study on the effect of the nature of the side chain, of the base, and of the acyl group on the course of the enzymatic synthesis is required. Such investigations are now in progress.

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RECEIVED JULY 6, 1948

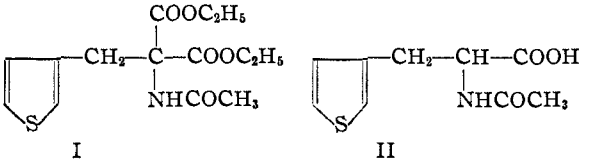
THE SYNTHESIS OF β-3-THIENYLALANINE

Sir:

Due to the current interest in metabolite–antimetabolite relations, and in particular to the discovery by du Vigneaud and associates[1,2] that β-2-thienylalanine functioned as a phenylalanine anti-metabolite with yeast, we are prompted to describe an isomer of this compound, β-3-thienylalanine, which we have prepared for testing as a phenylalanine antagonist.

The synthesis involves the reaction of 3-thienyl bromide with sodioacetamidomalonic ester to form 3-thenylacetamidomalonic ester (I). The 3-thenyl bromide was prepared by the peroxide-catalyzed reaction of N-bromosuccinimide with 3-methylthiophene, as previously described.[3] I melted at 90–91° after recrystallization from water.

Anal. Calcd. for $C_{14}H_{19}O_5NS$: S, 10.20. Found: S, 9.92. Alkaline hydrolysis of I, followed



I II

by acidification and heating, yielded N-acetyl-β-3-thienylalanine (II), m. p. 148–149°. *Anal.* Calcd. for $C_9H_{11}O_3NS$: S, 15.03; N, 6.57. Found: S, 15.14; N, 6.82.

β-3-Thienylalanine was prepared by complete hydrolysis of I in barium hydroxide, acidification with sulfuric acid, decarboxylation, and neutralization with barium carbonate. The water solution thus obtained was concentrated to dryness, and the residue recrystallized from water. β-3-Thienylalanine precipitated as fine white crystals, which browned at 260° and melted with decomposition from 265–267°. *Anal.* Calcd. for $C_7H_9O_2NS$: S, 18.71; N, 8.19. Found: S, 18.43; N, 8.10.

Complete details on the synthesis and biological testing of this compound will be published at a later date.

(3) Campaigne and LeSuer, THIS JOURNAL, 70, 1555 (1948).

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RECEIVED MARCH 13, 1948

THE PREPARATION AND POLYMERIZATION OF MONOMERIC CYCLIC DISULFIDES

Sir:

Carothers extensively described the reversible polymerization relationships existing between monomeric cyclic anhydrides,[1] esters,[2] and formals.[3] Patnode and Wilcock[4] recently described the reversible conversion of methyl polysiloxanes to cyclic compounds. We have found that a similar reversible polymerization is possible between high-molecular weight disulfide polymers and the corresponding monomeric disulfide ring.

Steam distillation of aqueous dispersions of disulfide polymers yields very small amounts of

(1) du Vigneaud, McKennis, Simonds, Dittmer and Brown, *J. Biol. Chem.*, 159, 385 (1945).

(2) Dittmer, Ellis, McKennis and du Vigneaud, *ibid.*, 164, 761 1946).

(1) J. W. Hill and W. H. Carothers, THIS JOURNAL, 55, 5023 (1933).

(2) W. H. Carothers, G. L. Dorough and F. J. Van Natta, *ibid.*, 54, 761 (1932).

(3) J. W. Hill and W. H. Carothers, *ibid.*, 57, 925 (1935).

(4) W. Patnode and D. F. Wilcock, *ibid.*, 68, 358 (1946).