slight modifications. The mixture of 72 g. of hippuric acid, 33 g. of anhydrous sodium acetate and 200 ml. of acetic anhydride was maintained at 30° under a reflux condenser while 250 ml. of propionaldehyde was added over a period of one hour. The mixture was then heated about forty-five minutes at 50–60° until an almost clear orange solution resulted. Decomposition with ice yielded a semi-crystalline mass which was washed several times with ice water. The small amount of oil present was dissolved by adding 300 ml. of 70% ethanol and the resulting mixture was filtered by suction to give light yellow crystals. These crystals were sucked as dry as possible, washed several times with water and air dried. The yield of crude azlactone was 30–33 g., m. p.[3] 79–81°. Recrystallization from 50% ethanol gave white needles, m. p. 81–83°.

Anal. Calcd. for $C_{12}H_{11}NO_2$: N, 6.96. Found: N, 6.94.

If the temperature of the reaction were allowed to rise above 60° or the time of heating were prolonged, the yield suffered markedly and the majority of the resultant product was the dark red oil. The crude material was entirely satisfactory for the next step.

α-Benzoylamino-β-benzylmercapto-*n*-valeric Acid.—To a solution of 0.67 g. of sodium in 140 ml. of dry methanol was added 17.2 g. of benzyl mercaptan. Then a solution of 27 g. of 2-phenyl-4-*n*-propylidene-5-oxazolone in 140 ml. of dry benzene was added, with stirring, over a period of one hour. The mixture was allowed to stand at room temperature for fourteen hours. The product was isolated as described for the butyric acid derivative[1] except that the mixture was stirred and heated on the steam-bath for five hours. It was chilled and diluted with 250 ml. of water. A dark brown, gummy mass precipitated and tended to solidify after standing for several hours. It was washed with water and dissolved in 150 ml. of benzene. The water which had been entrapped was removed and the benzene solution was filtered. The solution was diluted with 500 ml. of gasoline causing the separation of an oil that soon solidified into light gray crystals. The yield of crude α-benzoylamino-β-benzylmercapto-*n*-valeric acid was 15 g., m. p. 102–104°. A small sample was recrystallized from the benzene–gasoline mixture, m. p. 103–105°.

Anal. Calcd. for $C_{19}H_{21}NO_3S$: N, 4.08. Found: N, 3.84.

The crude material was sufficiently pure for use in the following step.

A larger run from 60 g. of the oxazolone yielded 60 g. of the acid melting at 102–104°.

α-Amino-β-benzylmercapto-*n*-valeric Acid.—A mixture of 30 g. of α-benzoylamino-β-benzylmercapto-*n*-valeric acid, 230 ml. of commercial formic acid (87%), 230 ml. of concentrated hydrochloric acid and 230 ml. of water was heated under reflux for twelve hours. After the mixture had been cooled in an ice-bath, starting material (15 g.) was removed by filtration. The clear filtrate was evaporated to dryness *in vacuo* and the residue was taken up in 500 ml. of water. A small amount of a brown insoluble substance was removed by filtration. The filtrate was made slightly alkaline with ammonium hydroxide and then was evaporated to remove excess ammonia. α-Amino-β-benzylmercapto-*n*-valeric acid crystallized in white plates, yield 7.5 g., m. p. 172–174°. A small sample was recrystallized from water, m. p. 177–179°.

Anal. Calcd. for $C_{12}H_{17}NO_2S$: N, 5.87. Found: N, 5.98.

α-Amino-β-mercapto-*n*-valeric Acid Hydrochloride.—Sodium (about 2.5 g.) in small pieces was added with vigorous stirring to a solution of 7 g. of the above acid in 100 ml. of liquid ammonia. The metal was added until a deep blue color persisted. This color was discharged by the addition of sufficient solid ammonium chloride. The ammonia was then allowed to evaporate, eventually at reduced pressure to remove final traces. The residue was washed with ether and again evaporated *in vacuo*. The white product was dissolved in 50 ml. of dilute hydrochloric acid and the solution was extracted twice with 50-ml. portions of ether. Again the solution was evaporated to dryness *in vacuo*.

This residue was extracted with 150 ml. of absolute ethanol and the ammonium and sodium chlorides were removed by filtration. The alcohol solution was evaporated to dryness at reduced pressure. The light yellow solid was redissolved in 100 ml. of absolute ethanol and this solution was treated with decolorizing charcoal, filtered and evaporated *in vacuo*.

The white crystalline solid was dissolved in 75 ml. of absolute ethanol. Anhydrous ether was added until a slightly cloudy solution resulted. After the mixture had stood for fiteen minutes, the amino acid hydrochloride began to crystallize in small, white platelets. The mixture was then chilled for several hours and filtered. The yield of white, crystalline α-amino-β-mercapto-*n*-valeric acid hydrochloride was 3 g., m. p. 154–156°. More acid was obtained by working up the ether–ethanol mother liquor. The product gave a strong nitroprusside test to indicate the presence of the sulfhydryl rather than sulfide group.

After two further recrystallizations, the melting point was 163–165°. The nitroprusside test was still strongly positive.

Anal. Calcd. for $C_5H_{11}NO_2S \cdot HCl$: N, 7.54. Found: N, 7.32.

Throughout this synthesis no attempt was made to separate the two theoretically possible racemic modifications in pure form or to determine if more than one form were present.

THE LILLY RESEARCH LABORATORIES
ELI LILLY AND COMPANY
INDIANAPOLIS, INDIANA
JOSEPH CORSE[4]
E. C. KLEIDERER
QUENTIN F. SOPER

RECEIVED SEPTEMBER 2, 1947

(4) Present address, University of California at Los Angeles, Los Angeles, California.

4-Fluoroanthranilic Acid

4-Fluoro-2-nitrotoluene.—3-Nitro-4-toluidine (228 g., 1.5 moles)[1] was suspended in a mixture of 313.5 cc. of concd. hydrochloric acid and 450 cc. of water, chilled to 0° and diazotized using 130 g. of sodium nitrite (as a 35% solution). The filtered diazonium solution was stirred at 0° while 451 g. of 40% fluoboric acid solution was added (*ca.* ten minutes), and stirred for half an hour. After washing (ice-water, methanol, and ether), the cream-colored crystalline diazonium borofluoride was dried, first in air, then *in vacuo* (over paraffin and phosphoric anhydride); yield, 202 g. (54%).

The diazonium borofluoride was decomposed by heating it alone or mixed with an equal weight of acid-washed sand in an apparatus with wide-bore tubing (25 mm.) connected to several traps (*cf.* ref. 2). All products of the reaction, including the residual ashes in the decomposition flask, were combined and distilled with steam. The distillate was extracted with ether, and the extracts freed of phenolic matter by washing with 5% sodium hydroxide and saturated salt solution. After drying (Na_2SO_4), the extract was fractionated[3]; 125–134 g. (67–71%) of yellow liquid was collected at 75–76° (5 mm.) or 108–109° (23 mm.), $n^{25}D$ 1.5212. 4-Fluoro-2-nitrotoluene was previously obtained by the nitration of 4-fluorotoluene[4]; b. p. 102.4° (20 mm.), $n^{25}D$ 1.51997.

5-Fluoro-2-acetotoluidide.—Reduction of 4-fluoro-2-nitrotoluene by the method of West,[5] using aqueous

(1) Noelting and Collin, *Ber.*, **17**, 263 (1884).

(2) Flood, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, New York, N. Y., 1943, p. 295.

(3) A 25 cm. vacuum-jacketed Vigreux column was used in the distillation.

(4) Desirant, *Bull. sci. acad. roy. Belg.*, **19**, 325 (1933); *C. A.*, **27**, 4781 (1933).

(5) West, *J. Chem. Soc.*, 494 (1925).

(3) Melting points were determined by means of a Fisher–Johns melting-point block.

methanol as the milieu, gave the pure amine in yields of 80–86%. 5-Fluoro-2-toluidine was a colorless liquid, b. p. 100–101° (16 mm.),[3] $n^{25}D$ 1.5379.

Anal. Calcd. for C_7H_8FN: N, 11.21. Found: N, 11.15.[6]

The amino compound was interacted with acetic anhydride to give 5-fluoro-2-acetotoluidide in 96% yield. It separated from aqueous alcohol in the form of white prismatic needles, m. p. 133.5–134°.

Anal. Calcd. for $C_9H_{10}FNO$: N, 8.38. Found: N, 8.54.

4-Fluoranthranilic Acid.—Five and three-tenths grams (0.0317 mole) 5-fluoro-2-acetotoluidide was added to a solution (at 75–80°) containing 10.3 g. of magnesium sulfate heptahydrate and 14.5 g. of potassium permanganate in 750 cc. of water. The mixture was stirred at 75–80° for two hours, then filtered and the filtrates acidified with dilute sulfuric acid. When crystallized from aqueous ethanol, 4.95 g. (79%) of 4-fluoroacetylanthranilic acid was obtained; the white platelets melted 209–209.5°.

Anal. Calcd. for $C_9H_8FNO_3$: N, 7.10. Found: N, 7.04.

Hydrolysis of the acetyl compound with boiling 6 *N* hydrochloric acid or 6 *N* sodium hydroxide gave 78–85% yields of 4-fluoroanthranilic acid. The compound crystallized from water as white needles of melting point 192.5–193°.

Anal. Calcd. for $C_7H_6FNO_2$: C, 54.19; H. 3.90; N, 9.03. Found: C, 54.07; H, 3.65; N, 9.11.

(6) All analyses were carried out under the direction of Mr. M. E. Auerbach in the analytical laboratories of this Institute.

THE STERLING–WINTHROP RESEARCH INSTITUTE
RENSSELAER, NEW YORK
EDGAR A. STECK
LYNN T. FLETCHER

RECEIVED SEPTEMBER 13, 1947

Ethyl α-Ethoxalylvalerate

The Claisen reaction of diethyl oxalate with ethyl valerate[1] was carried out in dry benzene using commercial sodium methoxide in essentially the manner described for ethyl α-ethoxalylpropionate.[2] An excess of ethyl valerate was used. The crude ester was difficult to distil satisfactorily, and the pure ethyl α-ethoxalylvalerate was obtained in yields of 20–24.5%, based upon diethyl oxalate employed; a 25-cm. vacuum-jacketed Vigreux column was required in the distillation, b. p. 78–80° (0.2 mm.), $n^{25}D$ 1.4319. This compound was prepared, but not obtained in a pure condition, by Adickes and Andresen.[3]

Anal. Calcd. for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found[4]: C, 57.18; H, 7.66.

To determine the position of entrance of the ethoxalyl group, a sample of the ester was heated at 165–175° with powdered glass during three hours. Decarbonylation led to a 53% yield of diethyl propylmalonate, b. p. 78–80° (2 mm.), $n^{25}D$ 1.4201. An authentic sample of the malonic ester boiled at 79–81° (2 mm.), $n^{25}D$ 1.4206.

The **2,4-dinitrophenylhydrazone**, prepared in the customary fashion, separated from 80% alcohol in the form of golden leaflets, m. p. 87–87.5° (lit.[3] value, 85–86°—only this derivative was prepared, using crude ester).

Anal. Calcd. for $C_{17}H_{22}N_4O_8$: N, 13.65. Found: N, 13.80.

(1) Purchased from Northeastern Chemical Co., Wauwatosa, Wis.
(2) Steck, Halloćk and Holland, THIS JOURNAL, **68**, 131 (1946).
(3) Adickes and Andresen, *Ann.*, **555**, 55 (1943).
(4) All analyses were carried out under the direction of Mr. M. E. Auerbach in the analytical laboratories of this Institute.

THE STERLING–WINTHROP RESEARCH INSTITUTE
RENSSELAER, NEW YORK
EDGAR A. STECK
ARNOLD J. HOLLAND

RECEIVED SEPTEMBER 13, 1947

COMMUNICATIONS TO THE EDITOR

THE STRUCTURE OF CITRININ

Sir:

Hetherington and Raistrick[1] degraded citrinin (I, $C_{13}H_{14}O_5$) with dilute acid to II ($C_{11}H_{16}O_3$), which was fused with alkali to give III ($C_9H_{12}O_2$), which in turn was methylated and oxidized to two carboxylic acids IV ($C_{11}H_{14}O_4$) and V ($C_{10}H_{12}O_4$). The compound 4-methyl-5-ethylresorcinol has now been synthesized by two methods, and a comparison of this substance with III (prepared from citrinin) shows that they have the same structure. Two acids, 2-ethyl-4,6-dimethoxybenzoic acid and 2-methyl-3,5-dimethoxybenzoic acid have also been synthesized, and their properties correspond to those reported for IV and V, respectively. No degradation products of citrinin have been previously synthesized.

(1) Hetherington and Raistrick, *Trans. Roy. Soc.* (London), **B220**, 1–10 (1931).

Formylation of 5-ethylresorcinol[2] with zinc cyanide and hydrogen chloride produced 2-ethyl-4,6-dihydroxybenzaldehyde[3]; the two phenolic hydroxyl groups were methylated to give 2-ethyl-4,6-dimethoxybenzaldehyde, which was in turn oxidized to 2-ethyl-4,6-dimethoxybenzoic acid, m. p. 99–100° (Hetherington, *et al.*,[1] reported a melting point of 98–99° for IV).

Anal. Calcd. for $C_{11}H_{14}O_4$: C, 62.84; H, 6.71. Found: C, 62.76; H, 6.71.

Reduction of 2-ethyl-4,6-dimethoxybenzaldehyde to 2-methyl-3,5-dimethoxyethylbenzene, followed by demethylation of the two methoxyl groups produced 4-methyl-5-ethylresorcinol, m. p. 67–69°. A mixed melting point of this compound

(2) This compound was prepared by the procedure of Asahina and Ihara, *J. Pharm. Soc. Japan*, **48**, 28 (1928).
(3) This substance had been prepared previously by Geissman and Tulagin (unpublished work).