Oxidation of Trithioallophanate Esters. A. With Iodine.—While chilling a solution of 2.0 g. (0.012 mole) of methyl trithioallophanate in 50 ml. of absolute ethanol a solution of 3.1 g. (0.012 mole) of iodine in 100 ml. of ethanol was added with shaking over a 10-minute period. After standing at 0° for an hour, the yellow precipitate was filtered, washed with cold ethanol and dried in a vacuum desiccator. The β-hydroxyethyl homolog was prepared in the same fashion, excess iodine being removed from the product with 40–60° petroleum ether washes. The ethyl homolog was prepared by adding solid iodine to a solution of ethyl trithioallophanate. The product was triturated three times with hot chloroform to remove excess iodine.

B. With Bromine.—To a chilled suspension of 4.5 g. (0.027 mole) of methyl trithioallophanate in 100 ml. of chloroform was added with shaking a solution of 4.4 g. (0.027 mole) of bromine in 25 ml. of chloroform over a period of 15 minutes. The dark yellow product was digested in hot ethanol which removed the dark color and left a pale yellow solid. The ethyl homolog was prepared in similar fashion; the reaction product was repeatedly triturated with hot chloroform to remove impurities. The isopropyl and *n*-propyl derivatives were prepared as above. Being soluble in chloroform, they were precipitated as orange oils by the addition of 40–60° petroleum ether. Repeated extractions with petroleum ether gave yellow solids; the isopropyl derivative was recrystallized from chloroform and 40–60° petroleum ether, the *n*-propyl derivative from ethanol. The *n*-butyl homolog was prepared by the method used for the methyl derivative.

C. With Chlorine.—The procedure for the oxidation of *n*-butyl trithioallophanate with chlorine was the same as that for bromine oxidation except that carbon tetrachloride served as solvent. The lumpy yellow product was washed successively with dioxane, ethanol and 40–60° petroleum ether.

D. With Sulfuric Acid.—A paste of 6 ml. of concd. sulfuric acid and 2.0 g. (0.012 mole) of methyl trithioallophanate was stirred five minutes, filtered through Dicalite and diluted with 30 ml. of water, 100 ml. of acetone and 400 ml. of ether. The volume of the aqueous layer was reduced two-thirds by repeated ether extractions, then acetone and ether were added to the remaining aqueous layer until solution was effected. Refrigeration produced pale yellow granular crystals.

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Thiosemicarbazones of *p*-Acetaminocinnamaldehyde and β-2-Thienylacrolein

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In pursuing a program dealing with the chemotherapy of tuberculosis, *p*-acetaminocinnamaldehyde and β-2-thienylacrolein thiosemicarbazones have been prepared. The former is a vinylog of *p*-acetaminobenzaldehyde thiosemicarbazone (Tibione)[1]; a compound recognized as an effective tuberculostatic agent. Likewise, 2-thenaldehyde thiosemicarbazone has been reported to have a high order of activity against the tubercle bacillus *in vitro*.[2,3] A later report[4] indicated that this compound afforded weak protection to mice infected with tuberculosis.

As the similarity in physical properties and chemical reactivity of a compound and its vinylog is well known,[5] it would appear that this correlation might be extended to include physiological action. Continued investigations into the pharmacology of vinylogous substances appeared to be warranted on the basis of interesting results previously obtained.[6]

The following points about the chemical work were observed: (1) In the preparation of *p*-acetaminocinnamaldehyde, dilute alcohol was found to be a more convenient solvent for recrystallization than hot water which was used by previous workers.[7] (2) The addition of a small quantity of either hydrochloric or acetic acid facilitated the reaction of thiosemicarbazide with the aldehyde, so that it was complete in 20–30 minutes. This is in contrast to the 6–8 hours reported by others.[3]

The compounds described in this paper have been submitted to Parke, Davis and Company for pharmacological evaluation.

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Experimental[8]

Intermediate Carbonyl Compounds.—*p*-Acetaminocinnamaldehyde was prepared according to the procedure of Russell, Todd and Waring,[7] modifying the procedure only in regard to the solvent used in recrystallization as reported above. These authors did not report a yield; the crude yields obtained in the present work ranged from 15–20%.

β-2-Thienylacrolein was prepared according to the method of Keskin, Miller and Nord.[9]

Thiosemicarbazones.—The thiosemicarbazones were prepared by the general procedure as described by Nobles and Burckhalter,[10] using either hydrochloric or acetic acid to augment the reaction. Both of the products were recrystallized from 50% ethanol.

***p*-Acetaminocinnamaldehyde Thiosemicarbazone.**—By the foregoing procedure, a 92% yield of light orange solid was obtained, m.p. 207°. *Anal.* Calcd. for $C_{12}H_{14}ON_4S$: C, 54.94; H, 5.39. Found: C, 55.25; H, 5.54.

β-2-Thienylacrolein Thiosemicarbazone.—By the same general procedure, a 90% yield of orange solid was obtained, m.p. 102°. *Anal.* Calcd. for $C_8H_9N_3S_2$: C, 45.48; H, 4.29. Found: C, 45.00; H, 4.47.

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Vinylidene Cyanide. IV. A Dienophile in the Diels–Alder Reaction[1]

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When vinylidene cyanide (I) became available as a result of the synthetic methods described in the earlier papers of this series,[2] it became of

(1) Presented before the Division of Organic Chemistry of the American Chemical Society 124th Meeting, Chicago, Ill., September, 1953.

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