was twice recrystallized from methanol giving 1.5 g. (21%) of 2,3,4,5-tetrachlorobiphenyl, m.p. 88–89°. On admixture with an authentic sample[8] the melting point was undepressed.

Anal. Calcd. for $C_{12}H_6Cl_4$: C, 49.30; H, 2.05; Cl, 48.70. Found: C, 49.59; H, 2.39; Cl, 48.41.

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Some Derivatives of 3-Thenaldehyde

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3-Thenaldehyde[2] has been condensed with acetone to yield 4-(3-thienyl)-3-butene-2-one in approximately 60% yield, and this substance has been converted to its thiosemicarbazone.

Previously, it had been demonstrated that the thiosemicarbazone of 4-(2-thienyl)-3-buten-2-one was capable of completely inhibiting the *in vitro* growth of *Mycobacterium tuberculosis* H37RV in a relatively low concentration.[3] Thus, it was thought to be of interest to prepare the corresponding 3-isomer in order that its activity might be compared with that of the 2-derivative. Preliminary results have indicated that the 3-isomer possesses significantly higher *in vitro* antitubercular activity than does the corresponding 2-substituted thiophene derivative. This may be seen from an examination of the contents of Table I.

TABLE I

Organism	Strain	γ/ml. causing complete inhibition: 2-Thienyl	3-Thienyl	Isonicotinic acid hydrazide
M. tuberculosis	H37RV	3.13	0.16	0.024
M. tuberculosis	INH-Resistant	..	.08	...
M. tuberculosis	Streptomycin resistant	..	.08	...

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Experimental[4,5]

4-(3-Thienyl)-3-buten-2-one.—To a mixture of 3-thenaldehyde (prepared according to the modified procedure of Angyal, see footnote 2), 43.5 g. (0.75 mole) of acetone and 30 ml. of water was added slowly, with stirring, 10 ml. of 10% sodium hydroxide solution. During the addition and immediately thereafter, the temperature was maintained at 20–25° by external cooling and constant stirring. After all of the alkali had been added, the mixture was stirred for 2.5 hours at room temperature. Then, cold dilute hydrochloric acid was added until the mixture was acid to litmus. The mixture was then extracted with benzene and the benzene extract dried over anhydrous potassium carbonate. The benzene was distilled at atmospheric pressure. The residue was distilled *in vacuo*. The material which distilled at 148–152° (20–24 mm.) solidified to a yellow mass on standing; yield 24 g. (63%), m.p. 52–53°. *Anal.* Calcd. for C_8H_8OS: C, 63.13; H, 5.29. Found: C, 63.31; H, 5.46.

4-(3-Thienyl)-3-buten-2-one Thiosemicarbazone.—This compound was prepared by the general method described by Nobles and Burckhalter[6] using a few drops of hydrochloric acid to facilitate the reaction. The crude product was recrystallized from 50% ethanol, m.p. 128–129°. *Anal.* Calcd. for $C_9H_{11}N_3S_2$: C, 47.97; C, 4.92. Found: C, 48.15; H, 5.03.

(1) Gustavus A. Pfeiffer Memorial Research Fellow, 1955–1956.

(2) E. Campaigne, R. C. Bourgeois and W. C. McCarthy, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., Vol. 33, p. 93, 1955. Our sample was prepared by the procedure of S. J. Angyal, *et al.*, *J. Chem. Soc.*, 1742 (1953), developed for 2-thenaldehyde.

(3) Unpublished results, courtesy of Dr. L. M. Long, Parke, Davis and Co., Detroit, Michigan.

(4) All melting points are uncorrected.

(5) Carbon and hydrogen analyses by Weiler and Strauss, Oxford, England.

(6) W. L. Nobles and J. H. Burckhalter, *J. Am. Pharm. Assoc.*, **42**, 176 (1953).

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The Synthesis of β-Cyclopropyl-α-aminopropionic Acid

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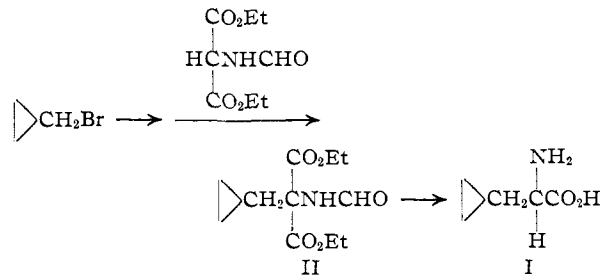
It has been shown that the interchange of a vinylene group and a sulfur atom frequently results in antimetabolitic action.[2] Similarly, it has been found that an acetylene group can also be used in place of a sulfur atom.[3]

In an extension of these exchanges, a cyclopropylene group has been introduced in place of a sulfur atom to form β-cyclopropyl-α-aminopropionic acid (I) to continue the allyl- and propargylglycine series based on cysteine. Compound (I) also may be considered a possible precursor of naturally occurring amino acids in that an organism might open the cyclopropyl ring and produce either norleucine or the essential amino acid leucine.[4]

We have now synthesized I and it has been found to be a potent antagonist to *E. coli* A.T.C.C.



(1) Taken from the Master's thesis of John W. Rowe, University of Colorado, 1952.

(2) (a) K. Dittmer, G. Ellis, H. McKennis and V. du Vigneaud, *J. Biol. Chem.*, **164**, 761 (1946); (b) R. G. Garst, E. Campaigne and H. G. Day, *ibid.*, **180**, 1013 (1949); (c) K. Dittmer, H. L. Goering, I. Goodman and S. J. Cristol, THIS JOURNAL, **70**, 2499 (1948).

(3) (a) H. Gershon, J. S. Meek and K. Dittmer, *ibid.*, **71**, 3573 (1949); (b) H. Gershon, J. Shapira, J. S. Meek and K. Dittmer, *ibid.*, **76**, 3484 (1954).

(4) α-Aminocyclopropylacetic acid likewise might be converted by an organism to the essential amino acid valine. α-Aminocyclopropylacetic acid has been synthesized and did not affect the growth of a wild type of *Neurospora crassa*. However, this amino acid was not tested with any organism as a possible substitute for valine; *cf.* P. H. Lowry, THIS JOURNAL, **74**, 1355 (1952).