**5-Cyano-8-acetoxyquinoline.**—A solution of the oxime (100 mg.) in acetic anhydride (0.5 ml.) was heated at 140° for 2 hours and poured, after cooling, into ice-water to give grey-white needles (100 mg.). Crystallization from benzene, yielded almost colorless prismatic needles, m.p. 153°. The solution in dilute ethanol gave no color reaction with ferric chloride.

*Anal.* Calcd. for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.80. Found: C, 67.91; H, 3.77.

**5-Cyano-8-quinolinol.**—A solution of 5-cyano-8-acetoxyquinoline (200 mg.) in 10% sodium carbonate (15 ml.) and ethanol (5 ml.) was refluxed for 2 hours. After removal of ethanol, the solution was acidified with acetic acid to give a colorless solid (quantitative yield) which crystallized from ethanol as prisms, m.p. 176.5–177°, mixed m.p. with the aldehyde (m.p. 178°) 158–165°. It gave a deep green color with ferric chloride and was readily soluble in dilute sodium carbonate.

*Anal.* Calcd. for $C_{10}H_6N_2O$: C, 70.60; H, 3.53. Found: C, 70.08; H, 3.73.

**Picrate.**—This formed as short prisms from ethanol; m.p. 251°.

*Anal.* Calcd. for $C_{10}H_6N_2O \cdot C_6H_3N_3O_7$: N, 17.54. Found: N, 17.56.

**Hydrochloride.**—This formed as yellowish white prismatic needles from dilute hydrochloric acid; m.p. 277° dec. It hydrolyzed in water.

*Anal.* Calcd. for $C_{10}H_6N_2O \cdot HCl$: N, 13.56. Found: N, 13.15.

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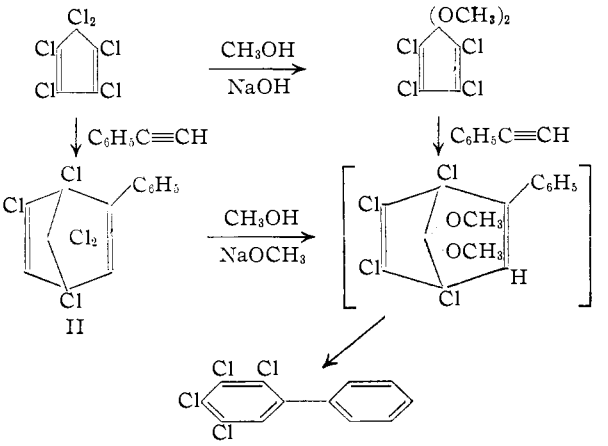
## Chemistry of Hexachlorocyclopentadiene. VI. Diels–Alder Adducts with Alkynes[1]

BY E. T. McBEE, J. D. IDOL, JR.,[2] AND C. W. ROBERTS

RECEIVED AUGUST 18, 1955

The Diels–Alder reaction with hexachlorocyclopentadiene (I) and various alkenes has been extensively studied.[3–7] The reactivity of I toward alkynes, which also may act as dienophiles,[8] however, has received very limited attention. Fields[4] has described an adduct prepared from I and 3-bromopropyne and the reaction of I with phenylacetylene has been investigated in this Laboratory and elsewhere.[7]

We have extended the reaction of I with alkynes to several other members of the series. 1-Hexyne, 1-heptyne and acetylenedicarboxylic acid gave monoadducts in yields varying from about 20–40% (see Table I).



It was observed that the dichloromethylene bridge in hexachlorocyclopentadiene–alkyne adducts exhibits a unique lability not found in the alkene adducts. Thus, when the phenylacetylene adduct (II) was treated in methanol with two equivalents of sodium methoxide 2,3,4,5-tetrachlorobiphenyl was obtained. The same biphenyl derivative has been isolated from the reaction product of 5,5-dimethoxytetrachlorocyclopentadiene and phenylacetylene, the adduct apparently constituting an intermediate in this reaction.[9] The same intermediate would theoretically result from treatment of the adduct II with two equivalents of methoxide. The fate of the bridge is uncertain since no fragments were isolated by us or previous workers.[9]

### Experimental[10]

**Preparation of Adducts.**—Equimolar portions of hexachlorocyclopentadiene[11] and the alkyne were mixed and refluxed (or heated to 150°, whichever was the lower temperature) for periods ranging from 24 to 120 hr. The unreacted starting materials and product were separated and purified by distillation. In the case of acetylenedicarboxylic acid which was insoluble in hexachlorocyclopentadiene, benzene was employed as the reaction medium and the acid was purified by recrystallization from a benzene–acetone mixture.

TABLE I
DIELS–ALDER ADDUCTS OF HEXACHLOROCYCLOPENTADIENE

| Alkyne | Adduct formula | B.p., °C. 2 mm. | $n^{20}D$ | Analyses, %[a] Carbon Calcd. | Carbon Found | Hydrogen Calcd. | Hydrogen Found | Chlorine Calcd. | Chlorine Found | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|
| $C_6H_5C{\equiv}CH$ | $C_{13}H_6Cl_6$ | 150–152 | 1.5498 | 41.60 | 41.91 | 1.60 | 1.90 | 56.90 | 56.51 | 21 |
| $n$-$C_4H_9C{\equiv}CH$ | $C_{11}H_{10}Cl_6$ | 124–128 | 1.5334 | 37.25 | 27.33 | 2.80 | 3.08 | 59.90 | 59.80 | 26 |
| $HOOCC{\equiv}CCOOH$ | $C_9H_2O_4Cl_6$ | 162–163[b] | | 27.85 | 27.84 | 0.51 | 0.76 | 55.02 | 54.97 | 45 |
| $n$-$C_5H_{11}C{\equiv}CH$ | $C_{12}H_{12}Cl_6$ | 160[c] | 1.5305 | 38.00 | 37.67 | 3.40 | 3.33 | ... | ... | 18 |

[a] Analyses, by Galbraith Micro-analytical Laboratories and Mrs. T. R. Yeh, Purdue University. [b] Melting point. [c] 5 mm. pressure

**2,3,4,5-Tetrachlorobiphenyl.**—Compound II, 1,4,5,6,7,7-hexachloro-2-phenylbicyclo[2.2.1]hepta-2,5-diene (9 g., 0.033 mole) was refluxed for 24 hr. in a solution of 3.6 g. (0.066 mole) of sodium methoxide in 75 ml. of methanol. The residue remaining after distillation of the solvent was dissolved in benzene and the solution decolorized with Norite. The filtrate was evaporated and the solid residue

(1) Paper V, E. T. McBee, H. Rakoff and R. K. Meyers, THIS JOURNAL, **77**, 4427 (1955).

(2) From a thesis submitted by James D. Idol, Jr., to the Graduate School of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, August, 1955.

(3) E. A. Prill, THIS JOURNAL, **69**, 62 (1947).

(4) E. K. Fields, *ibid.*, **76**, 2709 (1954).

(5) A. A. Danish, M. Silverman and Y. A. Tajima, *ibid.*, **76**, 6144 (1954).

(6) H. Rakoff, Ph.D. Thesis, Purdue University.

(7) Velsicol Corp., British Patent 614,931.

(8) H. L. Holmes in "Organic Reactions," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 60 et. seq.

(9) E. T. McBee, W. R. Diveley and J. E. Burch, THIS JOURNAL, **77**, 385 (1955).

(10) Melting points are uncorrected.

(11) Generously supplied by Hooker Electrochemical Co.

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

BY W. LEWIS NOBLES[1]

RECEIVED AUGUST 17, 1955

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 | ... |

**Acknowledgment.**—We would like to take this opportunity to acknowledge the support, in part, of this work by the Cyrus M. Warren Fund of the American Academy of Arts and Sciencies and by the American Foundation for Pharmaceutical Education. Also, our appreciation is expressed to Dr. L. M. Long, Parke, Davis and Co., for arranging for the pharmacological evaluation of these compounds.

### 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

BY JOHN S. MEEK AND JOHN W. ROWE[1]

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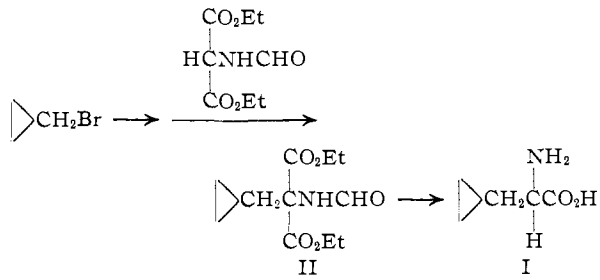
It has been shown that the interchange of a vinylene group and a sulfur atom frequently results in antimetabolitic action.[2] Similarly, it has been found that an acetylene group can also be used in place of a sulfur atom.[3]

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).