the mix was distilled at water-pump pressure to remove water azeotropically. The residual oil was fractionated at 0.2 mm. pressure and gave 11.6 g. of a viscous yellow oil which distilled at 103–106° and had $n^{25}$D 1.4537. The oil was dissolved in 10 ml. of absolute ethanol and neutralized with 13.7 ml. of 3.63 *N* alcoholic hydrochloric acid while maintaining the temperature below 20°. Solvent was removed *in vacuo* (temp. 40°) leaving 13 g. of a pale-yellow wax-like solid, m.p. 108–115°, which was submitted to analysis prior to purification for identification.

*Anal.* Calcd. for $C_{11}H_{26}ClN_3O_2$: N, 15.7. Found: N, 15.2, 15.0.

The crude salt (10 g.) was triturated with 15 ml. of acetone, filtered and washed two times with 5-ml. portions of acetone and dried *in vacuo;* yield 7.1 g., m.p. 122–124°. After two recrystallizations (isopropyl alcohol–ether), the preparation melted with no change at 126–127°.

*Anal.* Calcd. for $C_{11}H_{26}ClN_3O_4$: C, 49.92; H, 9.30; N, 15.02. Found: C, 49.62; H, 9.81; N, 15.84.

**Hydrolysis of N,N-Dimethyl-N′-isopropyl-N′-(2-nitroisobutyl)-ethylenediamine Hydrochloride.**—A solution of 1 g. of N,N-dimethyl-N′-isopropyl-N′-(2-nitroisobutyl)-ethylenediamine hydrochloride in 5 ml. of water was heated on the steam-bath for three hours, cooled and extracted with ether. The aqueous layer was concentrated *in vacuo* leaving a gummy residue which weighed 0.45 g. Trituration of this residue with acetone gave a crystalline solid identified by melting point (195–197°) and analysis as N,N-dimethyl-N′-isopropylethylenediamine dihydrochloride (II·2HCl).

*Anal.* Calcd. for $C_7H_{18}N_2 \cdot 2HCl$: C, 41.35; H, 9.89. Found: C, 41.94; H, 9.57.

The acetone filtrate from IIa was evaporated leaving a gummy residue (0.08 g.) which could not be purified for identification. Evaporation of the ether extract of the reaction mixture gave an oily residue, probably 2-nitroisobutanol or 2-nitroisobutene.

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# Chemistry of Hexachlorocyclopentadiene. V.[1] The Diels–Alder Reactions with Allylic and Halogen-containing Dienophiles

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Chloroprene and its homologs can be condensed with maleic anhydride or naphthoquinone at 100°; 1-chlorobutadiene and 2,3-dichlorobutadiene do not react under these conditions.[3] Although cyclopentadiene is more reactive than open-chain dienes, it was not predictable that hexachlorocyclopentadiene would undergo the Diels–Alder reaction at 100° with dienophiles such as maleic anhydride, *p*-benzoquinone, acrylonitrile and methyl vinyl ketone[4] or cyclopentadiene.[5,6] Similarly the fact that hexachlorocyclopentadiene would condense with allylic dienophiles and halogenated olefins which enter into the Diels–Alder reaction with the usual dienes only at elevated temperatures was unpredictable.

The adduct of hexachlorocyclopentadiene and allyl alcohol was prepared by refluxing the components with xylene. This adduct was converted to the acetate and propionate esters.

Certain halogen-containing olefins were found to undergo the diene synthesis with hexachlorocyclopentadiene at 200°. Of eighteen olefins investigated, only the following gave adducts: 1,2-dichloroethylene, 1,2-dibromoethylene, 1-chloropropene and 1,3-dichloropropene. Tetrachloroethylene, 1,1-dichloropropene, 1,2-dichloropropene, 1,1,2-trichloropropene, 1,2,3,3-tetrachloropropene, 1,1,2,3,3-pentachloropropene, 1,1,2-trichloro-3,3,3-trifluoropropene, 1,1,2,3-tetrachloro-3,3-difluoropropene and 2,3-dichlorohexafluoro-2-butene were unreactive at 200°. Vinylidene dichloride, tetrafluoroethylene, *asym*-dichlorodifluoroethylene and 2,3-dichloropropene underwent only dimerization or polymerization reactions. A comparison of the halogenated olefins indicates that two chlorine atoms on one double-bonded carbon inhibit the Diels–Alder reaction. Similarly, olefins with the structure $-\overset{|}{C}=CCl-R$ do not react. It is concluded that a halogenated dienophile to undergo reaction with hexachlorocyclopentadiene under the described conditions must have at least one hydrogen atom on each of the double bonded carbons.

## Experimental[7]

**1,2,3,4,7,7-Hexachloro-5-hydroxymethylbicyclo[2.2.1]-2-heptene.**—A mixture of allyl alcohol (65 g., 1.1 moles) and hexachlorocyclopentadiene (273 g., 1 mole) in 25 ml. of xylene was refluxed for 2 days. Low-boiling materials were removed by distillation, and the residual red-brown solid was decolorized and crystallized from ligroin (b.p. 90–100°). Two recrystallizations from the same solvent gave 178 g. (53%) of the colorless adduct, m.p. 162–165°. An additional crystallization raised the melting point to 164–165°.[6]

*Anal.* Calcd. for $C_8H_6Cl_6O$: Cl, 64.3. Found: Cl, 64.1.

**Acetate.**—The adduct (16 g.), when refluxed for 18 hours with acetic anhydride (8 g.) in benzene (25 ml.) yielded 14.5 g. (81%) of ester boiling at 144–146° (1 mm.). The analytical sample was fractionated from a small column and boiled at 154–155° (2 mm.), $n^{20}$D 1.5332.

*Anal.* Calcd. for $C_{10}H_8Cl_6O_2$: C, 32.2; H, 2.14. Found: 32.2; H, 2.06.

**Propionate.**—The same procedure furnished 87% of propionate ester, b.p. 160–161° (2 mm.), $n^{20}$D 1.5322.

*Anal.* Calcd. for $C_{11}H_{10}Cl_6O_2$: C, 34.1; H, 2.58. Found: C, 34.3; H, 2.56.

**1,2,3,4,7,7-Hexachloro-5-chloromethylbicyclo[2.2.1]-2-heptene.**—Allyl chloride (20 g., 0.26 mole) and hexachlorocyclopentadiene (70 g., 0.26 mole) were sealed in a Carius tube and heated to 125° for 18 hours. The tube was cooled and opened and the contents were distilled under reduced pressure to give 61 g. (68%) of adduct, b.p. 130–131° (3 mm.), which crystallized on standing to give a solid, m.p. 54–55°.[8]

*Anal.* Calcd. for $C_8H_5Cl_7$: Cl, 71.1. Found: Cl, 70.5.

1,2,3,4,7,7-Hexachloro-5-bromomethylbicyclo(2.2.1)-2-heptene was prepared in an analogous fashion to the chloride but at lower temperature (85–95°), m.p. 79–80°, in agreement with Fields.[6]

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[1] For paper IV, see E. T. McBee, H. E. Ungnade, H. Rakoff and K. Dinbergs, THIS JOURNAL, **77**, 4379 (1955).

[2] (a) A portion of a thesis by H. Rakoff submitted to Purdue University in partial fulfillment of the requirments for the degree of Doctor of Philosophy, 1950. (b) A portion of a thesis by R. K. Meyers submitted to Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1950.

[3] D. D. Coffman and W. H. Carothers, THIS JOURNAL, **55**, 2040 (1933).

[4] E. A. Prill, *ibid.*, **69**, 62 (1947).

[5] Velsicol Corporation, British Patent 614,931 (Dec. 30, 1948); S. H. Herzfeld, R. E. Lidov and H. Bluestone, to Velsicol Corporation, U. S. Patent 2,606,910 (Aug. 12, 1952).

[6] Subsequent to the completion of this work in 1950, the adducts of hexachlorocyclopentadiene with allyl alcohol, allyl chloride and allyl bromide have been described by E. K. Fields, THIS JOURNAL, **76**, 2709 (1954), and with vinyl chloride by H. Bluestone, U. S. Patent 2,676,132, April 20, 1954.

[7] All melting points are uncorrected. Analyses were done at Purdue University.

[8] Fields[6] reported a 43% yield b.p. 142–144° (3.7 mm.), but the isolation of no solid.

**1,2,3,4,6,7,7-Octachlorobicyclo[2.2.1]-2-heptene.**—A mixture of hexachlorocyclopentadiene (54 g., 0.2 mole) and *cis*-1,2-dichloroethylene (20 g., 0.2 mole) was heated for 25 hours in a sealed tube at 200°. The solid brown reaction product was crystallized from methanol to yield 28 g. (38%) of isomeric adducts, m.p. 170–190°.[9]

*Anal.* Calcd. for $C_7H_2Cl_8$: C, 22.7; H, 0.50. Found: C, 23.0; H, 0.49.

When *trans*-1,2-dichloroethylene was substituted for the *cis* isomer, only 20 g. (26%) of crude product was obtained under the same conditions.

**1,2,3,4,7,7-Hexachloro-5,6-dibromobicyclo[2.2.1]-2-heptene.**—Hexachlorocyclopentadiene (54 g., 0.2 mole) and 1,2-dibromoethylene (37 g., 0.2 mole) were heated in a sealed tube at 200° for 27 hours. The crude product (20 g.) was decolorized and crystallized from methanol. After three recrystallizations from methanol, there was obtained 15 g. (16%) of product, m.p. 210°.

*Anal.* Calcd. for $C_7H_2Br_2Cl_6$: total halogen (as chloride), 61.8. Found: total halogen, 61.9.

**1,2,3,4,6,7,7-Heptachloro-5-methylbicyclo[2.2.1]-2-heptene.**—A mixture of hexachlorocyclopentadiene (68 g., 0.25 mole) and freshly distilled 1-chloropropene (19 g., 0.25 mole) was heated in a sealed tube at 150–160° for 24 hours. Distillation of the reaction products gave 7 g. of 1-chloropropene, b.p. 35° (745 mm.), 38 g. of hexachlorocyclopentadiene (b.p. 83° (3 mm.)) and 33 g. of black residue, which solidified on cooling. Decolorization and crystallization from methanol furnished 6.5 g. of brown crystals, m.p. 165–180°. After several crystallizations from the same solvent, 4.7 g. (7.5%) of product, m.p. 197–198°, was obtained. When the same reactants were heated at 100°, no adduct was formed, while at 200° extensive decomposition took place.

*Anal.* Calcd. for $C_8H_5Cl_7$: C, 27.4; H, 1.40. Found: C, 28.2; H, 1.34.

**1,2,3,4,6,7,7-Heptachloro-5-chloromethylbicyclo[2.2.1]-2-heptene.**—Hexachlorocyclopentadiene (273 g., 1 mole) and 1,3-dichloropropene (111 g., 1 mole) were heated in a 1-liter flask, equipped with a reflux condenser, at 130° for 24 hours. Distillation of the reaction products yielded 73 g. of 1,3-dichloropropene (b.p. 106–113° (742 mm.)), 205 g. of hexachlorocyclopentadiene (b.p. 98–107°(7 mm.)) and 86 g. of black residue, which deposited brown crystals on standing. Decolorization and crystallization of this material from methanol gave 55 g. of yellow-brown solid, m.p. 55–65°. Several recrystallizations furnished 14 g. (15%) of colorless adduct, m.p. 78–80°.

*Anal.* Calcd. for $C_8H_4Cl_8$: C, 25.0; H, 1.04. Found: C, 25.5; H, 1.07.

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(9) The product may represent a mixture of *endo* and *exo* isomers.

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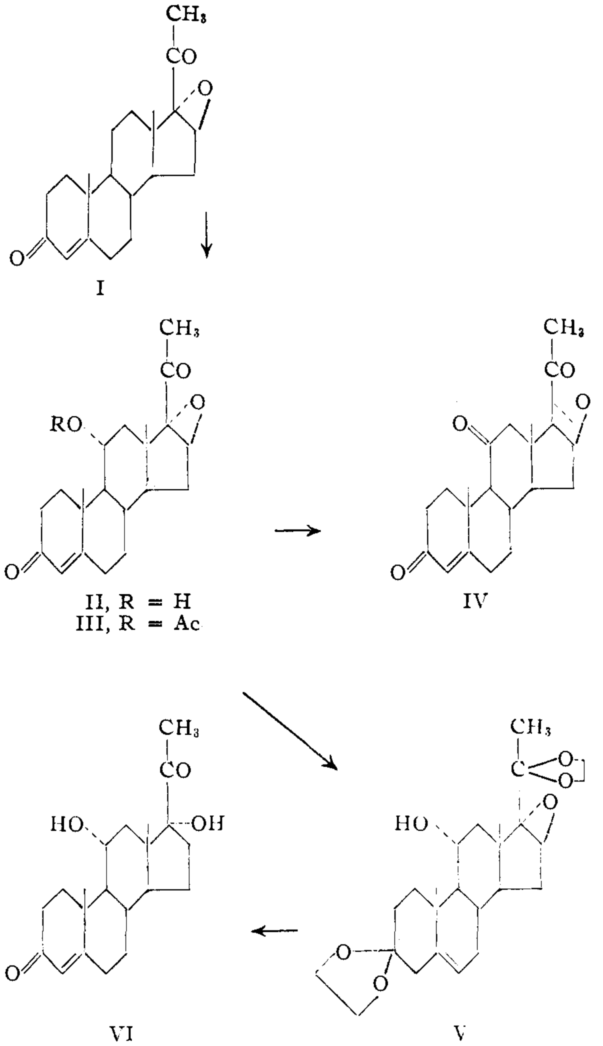
## Microbiological Transformation of Steroids. XIII. Oxygenation of 16α,17α-Oxidoprogesterone to 11α-Hydroxy-16α,17α-oxidoprogesterone by *Rhizopus Nigricans* Ehrb. (A.T.C.C. 6227b)[1]

BY D. H. PETERSON, P. D. MEISTER, A. WEINTRAUB, L. M. REINEKE, S. H. EPPSTEIN, H. C. MURRAY AND H. M. LEIGH OSBORN

RECEIVED AUGUST 31, 1954

In continuation of our studies on the enzymatic oxygenation of steroids with fungi of the genus *Rhizopus*, we wish to report the introduction of an 11α-hydroxyl group into 16α,17α-oxido-4-pregnene-3,20-dione (I) by *Rhizopus nigricans* Ehrb. (A.T.C.C. 6227b). The substrate I is readily prepared from sapogenins such as diosgenin by the method of Julian, Meyer and Ryden.[2] Upon incubation of I with a 24-hour growth of *Rhizopus nigricans* under conditions similar to those previously defined,[3] 11α-hydroxy-16,17-oxido-4-pregnene-3,20-dione (II) was obtained in 70–75% yield by direct crystallization. Compound II gave, on oxidation with chromium trioxide, 16,17-oxido-4-pregnene-3,11,20-trione (IV). Acetylation of II with acetic anhydride and pyridine yielded 11α-acetoxy-16,17-oxido-4-pregnene-3,20-dione (III). The latter compound has been synthesized chemically by the Schering group in a six-step synthesis from 3α,11α-diacetoxypregnan-20-one.[4] A comparison of the physical constants of our compound [m.p. 225–26°, $[\alpha]_D$ +113° ($CHCl_3$)] to those of the Schering compound [m.p. 217–18°, $[\alpha]_D$ +112.9° ($CHCl_3$)] would suggest that these two compounds are identical. However, the infrared spectra of the two


I

II, R = H
III, R = Ac

IV

VI

V

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(1) Paper XII of this series, THIS JOURNAL, **76**, 4050 (1954).

(2) P. L. Julian, E. W. Meyer and I. Ryden, *ibid.*, **72**, 367 (1950).

(3) D. H. Peterson, *et al.*, *ibid.*, **74**, 5933 (1952).

(4) H. L. Herzog, C. C. Payne, M. E. Tully and E. B. Hershberg, *ibid.*, **75**, 5751 (1953).