The Synthesis of Condensed Ring Compounds. XVII.[1] Total Synthesis of a 10a-Methyldodecahydrochrysene-1,4-dione (a 10-Methyl-D-homosteradiene-15,17a-dione)[2,3]

By Adam M. Gaddis and Lewis W. Butz

Excepting the configurations at the asymmetric centers, the structures of several wholly alicyclic steroid hormones are now completely established. No total synthesis of a wholly alicyclic steroid or D-homosteroid[4] with the functional groups of the hormones has been reported.

Dane and co-workers[5] have developed a procedure for the synthesis of benzenoid steroids and D-homosteroids which consists of Diels–Alder addition of a cyclenone to an α-vinylhydronaphthalene derivative. One of the reactions investigated was the addition of p-benzoquinone to I.[6] This


I
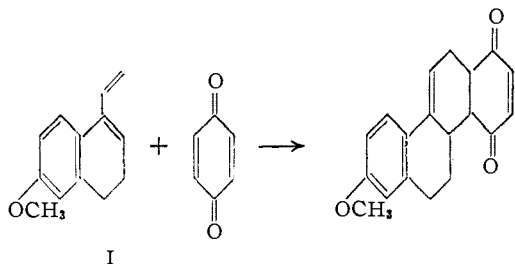
procedure has been varied by adding an open chain olefinic ketone to I and then forming a tetracyclic compound by intramolecular closing of the fourth ring.[7] Although the nature of the ring systems in these products from I was not demonstrated, there can be little doubt that they are steroids and D-homosteroids.

In the present work we followed the general procedure of Dane, but employed a methylvinylhexahydronaphthalene, of probable structure II, instead of I. The preparation of an adduct from II and p-naphthoquinone has already been reported.[8]

Catalytic hydrogenation of the ethynylmethylnaphthitenol described in a previous paper[8a] gave a methylvinylnaphthitenol, III, which was converted to a mixture of hydrocarbons containing II, or another derivative of 1-vinyl-1-naphthi-

tene such as IV, by reaction with phosphorus tribromide and distillation of the product.

II   III   IV
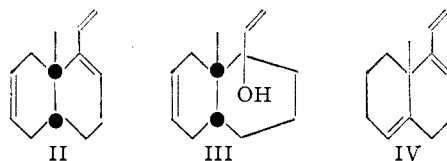
Combination of the triene II with p-benzoquinone gave the D-homosteroid V, or an isomer, which was converted to chrysene by way of an isomer which is very likely a diol such as VI.[9] The ultraviolet absorption spectrum of this isomer is in agreement with the formulation as VI, but may also be consistent with structures in which a benzene ring is conjugated with a C=C bond. In order to prevent a possible decomposition of the diol at the high temperature necessary for conversion to chrysene, in the sense of a reversal of the Diels–Alder addition which resulted in the formation of the naphthitenone,[8a] an attempt was made to hydrogenate the double bond which is probably in ring A. There was an apparent uptake of 1.4 moles of hydrogen. All of the product could not be crystallized, so the crude material was used for the next step. Suitable procedures for the conversion of such a partly alicyclic derivative of quinol containing an *angle*-methyl group to the aromatic hydrocarbon have not been described. We thought it best to apply first a deoxygenating procedure and then to heat with selenium. It is doubtful whether we achieved much deoxygenation in the first of these steps, but chrysene was obtained from the second.

V   VI
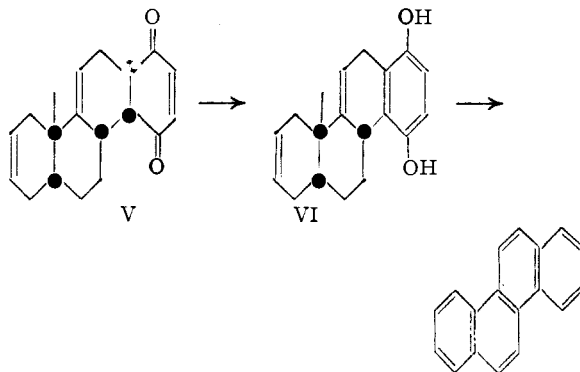
Reduction of V, called fraction A in the experimental part, with zinc and acetic acid[10] gave a

(1) For the preceding paper see This Journal, **69**, 924 (1947).

(2) The authors prefer names derived from chrysitane, as employed in an earlier paper (This Journal, **64**, 1311 (1942)), to those which include the prefix hydro. In deference to the wish of the Referee, the preferred names are being suppressed until it is possible to obtain the approval of an official committee.

(3) This work was supported by an allotment from the Special Research Fund (Bankhead–Jones Act of June 29, 1935). Not copyrighted.

(4) For nomenclature see Ruzicka and Meldahl, *Helv. Chim. Acta*, **23**, 364 (1940).

(5) Dane and Höss, *Ann.*, **552**, 113 (1942), and earlier papers.

(6) Dane, Höss, Bindseil and Schmitt, *Ann.*, **532**, 42 (1937).

(7) Goldberg and Müller, *Helv. Chim. Acta*, **23**, 831 (1940).
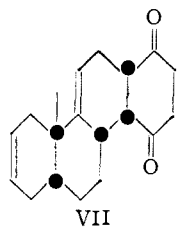
(8) Nudenberg and Butz, This Journal, **65**, 1436 (1943).

(8a) Gaddis and Butz, *ibid.*, **69**, 117 (1947).

(9) Fieser and Chang, *ibid.*, **64**, 2043 (1942).

(10) Alder and Stein, *Ann.*, **501**, 277 (1933).

10a-methyldodecahydrochrysene-1,4-dione (10-methyl-D-homosteradiene-15,17a-dione) which may be VII. The considerations which support this choice are as follows.


VII

The evidence for a 5,10-cis configuration in the ethynylmethylnaphthitenol, from which the compounds described in this paper were prepared, was cited in a previous paper[8a] and is convincing. It would be useful to know whether this carbinol could be separated into two 1-epimers, but this has not yet been investigated. The position of the C≡C bond in this carbinol and in the methylvinylnaphthitenol derived from it has not been established. However, in view of the apparent homogeneity of the 2,4-dinitrophenylhydrazone of the methylnaphthitenone[8a] and the unlikelihood that all of the methyl-7-naphthitenone formed by the Diels–Alder reaction would have isomerized, the C=C bond is very likely at position 7.

A disadvantage in the synthetic route to D-homosteroids described here is the low yield of methylvinylnaphthitadiene capable of reacting with p-benzoquinone. We have not investigated other methods for the preparation of tetracyclic compounds from the methylnaphthitenone and the two carbinols, having judged it better to establish first the structure of the D-homosteroids already obtained. For conversion of the methylvinylnaphthitenol to triene we have studied only the reaction with phosphorus tribromide followed by pyrolysis of the bromides. In a single experiment the effect of passing the vinylcarbinol over heated alumina was observed. The presence of more than 60% of a 1-vinyl-1-naphthitene, such as II or IV, in the part of the "triene" mixture which reacted with p-benzoquinone has been proven by conversion to chrysene. One C=C bond in this triene is at one of the positions 4, 5, 6, 7 or 8. Position 3 is excluded on the basis of the reaction with p-benzoquinone and the ultraviolet absorption. Although the structure of the other 40% of the adduct from the "trienes" and p-benzoquinone has not been established by conversion to a known compound, the transformation, in solution, of a large part of it to material very like the crystalline diol has been detected by the ultraviolet absorption spectrum exhibited by freshly prepared and old solutions. This observation, for which we are especially indebted to Mr. H. Bastron of this Laboratory,[11] suggests that the fraction B of the adduct (about 40% of the total) is a derivative of

chrysene which passes very easily to an ar-p-diol. Our inability to convert it to a crystalline diol may be due to the circumstance that several isomeric diols were produced by the procedure employed.[9] Also, in view of the well known displacing action of hydrogen halides upon C=C bonds, it is entirely possible that, though the C=C bond in the methylvinylnaphthitenol is at 7, it is at another position in the trienes. Thus the hydrocarbon which reacted with p-benzoquinone may have consisted of 80% of isomer IV and 20% of the 1,6-naphthitadiene.

With regard to the composition of the major part of the hydrocarbon mixture, which did not react with p-benzoquinone, the ultraviolet absorption curve is consistent with the structure VIII, the formation of which from the bromides from III could be readily understood. An interesting possibility, suggested by inspection of models, is structure IX. It may be that the atoms of the conjugated diene system are frozen by steric hindrance in the trans relationship shown which prevents Diels–Alder addition. Whether the unreactive trienes can be converted to reactive ones and whether they will react with p-benzoquinone under conditions other than those described in the experimental part has not been investigated.

VIII   IX
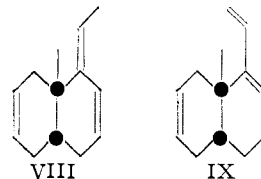
Using Linstead's notation, the most probable configurations of the D-homosteroids have been indicated in the formulas. In V, for example, the cis configuration is shown at positions 13,14[11a] since Alder and Stein[12] consider that all Diels–Alder reactions yield cis adducts. Although epimerization may have occurred, for example at C-13 by way of a mono-enol, this seems very unlikely. The configuration at C-8 is put cis to C-14 on the basis of the principle of addition with maximal clustering of multiple bonds.[12] The configuration at C-10 is put, on less sure ground, in the xx-relationship[13] to C-8, C-13 and C-14 because of the possible hindrance offered by the angle-methyl group to the formation of the other diastereoisomer. It may be that both diastereoisomers are formed.

The uncertainty of the position of the C=C bond in ring A or at C-5 has already been emphasized. Although it is important to determine its position, we recognize that wherever it is, passing to 3-substituted D-homosteroids, such as those

(11) We are indebted to Mr. Bastron, Animal Husbandry Division, for all of the spectrographic data in this paper.

(11a) The numbering of carbon atoms in this discussion is that universally employed for steroids. It has been applied previously to D-homosteroids by designating the last annular carbon atom C-18[2] or C-17a.[4]

(12) Alder and Stein, Angew. Chem., 50, 510 (1937).

(13) For configurational notation see Butz, Gaddis, Butz and Davis, J. Org. Chem., 5, 383, footnote (1940).

derived from natural steroids, is possible by known methods. The position of another C=C bond in ring C, or possibly at C-7, is also not established. No basis exists, however, in present knowledge, for the likelihood of a displacement from C-9 under the conditions of formation of V or its reductions with zinc and acetic acid.

The melting point of the adduct, which is probably V, changes within two days after isolation and small amounts of an isomer which melts much higher (291–294°) can be obtained by recrystallization. A possible formulation of the changes which the adduct underwent is as follows

V   →   VI
M. p. 166–170°   M. p. 291–294°

X   M. p. 207–208°

XI   XII
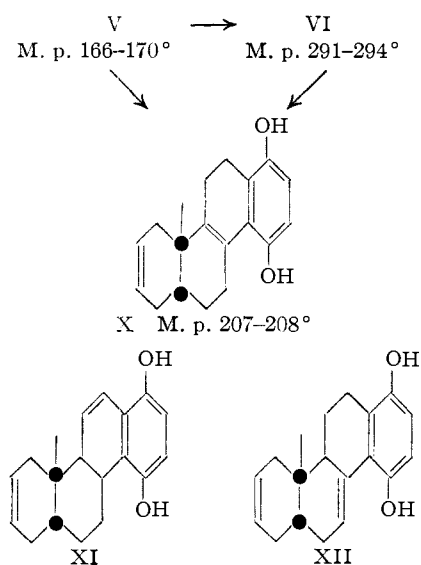
It is supposed that Fraction A consists chiefly of V which on standing changes slowly to VI. Both of these with the Fieser–Chang reagent[9] gave X, and possibly a little XI and XII.

If fraction A does consist chiefly of V, the structure of the compound reported here which most closely resembles the natural steroids is *r*-xxxxx-10a - methyl - 2,3,4a,4b,5,6,6a,7,10,10a,12,12a - dodecahydrochrysene-1,4-dione (*r*-xxxxx-10-methyl-2,9(11)-D-homosteradiene-15,17a-dione)(VII).[13]

Experimental[14]

10-Methyl-1-vinyl-5,10-*cis*?-7?-naphthiten-1-ol (III).— Ethynylmethylnaphthitenol[8a] (12.8 g.) in 105 ml. of ethanol was shaken with hydrogen in the presence of 0.8 g. of palladium–calcium carbonate catalyst[15] until 3% more than the volume calculated for the saturation of one double bond had been taken up. The mixture was warmed with a little carbon black and the catalyst was removed. After removal of the ethanol, distillation gave 11.6 g. (92%), b. p. 76–80° (0.3 mm.), $n^{20.4}$D 1.5226. This product gave no precipitate with ammoniacal silver nitrate.

10 - Methyl - 1 - vinyl - *cis*? - 1,7? - naphthitadiene (II) Mixed with One or More Other Hydrocarbons.—Since II, with any other isomers containing the 1-vinyl-1-naphthitene system, made up only a relatively small part of the whole product, the yields to be reported were calculated

with inclusion of the "triene" + *p*-benzoquinone step. The four best runs by way of the bromide gave 6.8, 7.8, 10.8 and 13.3% (72% of redistilled "trienes" × 18.5% of adduct from the "trienes".) of crude adduct (but free from *p*-benzoquinone) from the methylvinylnaphthitenol. In the single run in which the carbinol was dehydrated with alumina, this over-all yield was only 3.8%. The methyl-vinylnaphthitenol which gave the two highest yields of crude D-homosteroid was prepared from ethynylmethyl-naphthitenol which had been freed from most of the methylnaphthitenone by fractional distillation (n^{20}D 1.5250–1.5280). In these two instances distillation of the methylvinylnaphthitenol was omitted in order to minimize any isomerization.

A mixture of 11.6 g. (57 millimoles) of the methylvinyl-carbinol and 1.5 g. (19 millimoles) of pyridine was added dropwise to 5 g. (18.5 millimoles) of phosphorus tribromide, cooled in an ice-bath, during thirty minutes with shaking. After standing fifteen minutes at this temperature, the mixture was held at 40–50° for thirty minutes, about 15 ml. of ether was added, and the whole refluxed for one hour. Two days later the mixture was filtered, the gum washed with ether, the ether solution washed three times with water and three times with saturated sodium chloride, filtered through anhydrous sodium sulfate, and the ether removed at the water pump.

The system containing the residue from the ether solution was evacuated on the fourth day to a pressure of less than half a millimeter and a bath at 76° was applied. There was a soda-lime tube in the line between the receiver and cold-trap. The temperature of the bath was raised to 146° gradually during five hours. Slow distillation began after seventy-five minutes when the bath temperature was 115°. It was held at 115–125° for the next ninety minutes. The maximum vapor temperature was 76°. The colorless distillate (9.5 g.) was dissolved in ether, washed with sodium bicarbonate and saturated sodium chloride solutions, and dried over anhydrous sodium sulfate. After removal of the sodium sulfate and ether, distillation gave 7.1 g., b. p. 62–66° (0.45 mm.), $n^{19.4}$D 1.5298, and 1.5 g. boiling at 70–103° (0.45 mm.), $n^{18.6}$D 1.5373. The larger fraction gave 18.5% of adduct with *p*-benzoquinone. The higher boiling fraction gave a positive Beilstein test indicating the presence of bromine. Fractions of such high boiling point and refractive index have regularly been obtained and in one instance such a fraction was redistilled at 0.1 mm. pressure to give additional material, b. p. 57–58°, which was combined with the main fraction since it appeared to be free of halogen. The change in refractive index on redistillation was from 1.5340 to 1.5316. The composite had $n^{19.2}$D 1.5303 and represented the highest yield (77%) obtained in any run. However it gave only 14% of adduct with *p*-benzoquinone. The refractive indexes of the several preparations obtained by the pyrolysis of the bromides varied from 1.5267 to 1.5303. No correlation was noticed between these values and the yields of adduct with *p*-benzoquinone. The periods of time allowed for the various steps were changed from batch to batch; those described above happened to give the highest yield of adduct. Thus it is surely not necessary to let the products of the reaction with phosphorus tribromide stand in ether for two days.

Five grams of methylvinylnaphthitenol was distilled through an inclined tube, 560 × 20 mm., filled with freshly activated alumina, at 252–257° and 0.2 mm. pressure during forty minutes. The indicated temperature and pressure were maintained for five hours with intermittent passing of nitrogen through the tube, which was then allowed to stand evacuated overnight. On the following day the pressure was again brought to 0.2 mm., the tube was heated to 340° and held there for half an hour while nitrogen was passed in. The condensed products were taken up in ether, dried and distilled to give 3.4 g. (75%), b. p. 53–54° (0.1 mm.), n^{20}D 1.5241, ultraviolet absorption (see below); adduct with *p*-benzoquinone, only 5%.

In a preliminary communication[3] values were reported for the ultraviolet absorption spectra[11] of two batches of "triene." It must be emphasized that these values and

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(14) All melting points are corrected. Analyses by Arlington Laboratories, Fairfax, Virginia, or Dr. T. S. Ma, University of Chicago (M).

(15) Busch and Stöve, *Ber.*, **49**, 1064 (1916).

similar ones obtained since for other preparations do not represent a single compound. Probably the most homogeneous specimen is the "triene" recovered after combination of the reactive component with p-benzoquinone. In the following, the source of material, $\lambda_{max}(\text{Å.})$; ϵ, solvent; and $n^{20}D$ are given in that order. After reacting with p-benzoquinone, 2385, 11000, hexanes, 1.5284; from alumina, 2390, 5400, hexanes, 1.5241; via bromides,[8] 2380, 9400, hexanes (n_D not taken); via bromides,[8] 2380, 10000, ethanol, 1.5290. This last specimen absorbed the quantity of hydrogen calculated for three double bonds in the presence of Adams catalyst.[8] It may be that the chief component of the "triene" is an isomer with the 1-ethylidene-2-naphthitene group (λ_{max}, calcd. according to Woodward,[16] 2370 Å.; calcd. for II, 2270 Å.). Some data for related compounds[17] are not at variance with this suggestion. It seems unlikely that the "triene" contains any considerable quantity of isomers with two conjugated double bonds in one ring (λ_{max} 2700–2800 Å.)[18] although all the curves show a slight inflection at 2800–2900 Å.

Reaction of p-Benzoquinone with the Mixture of Trienes Containing a Derivative of 10-Methyl-1-vinyl-1-naphthitene.—Seven grams (40 millimoles) of "triene," b. p. 62–66° (0.5 mm.), $n^{19.4}D$ 1.5298, 1.45 g. (13 millimoles) of freshly sublimed p-benzoquinone and 18 ml. of benzene were held at 50° for twenty-four hours in a sealed tube filled with nitrogen. The next day a small quantity of black precipitate was removed by filtration, the filtrate was evaporated on a steam-bath with a stream of carbon dioxide until quinone began to sublime, the residue was left at 0° for one hour, 10 ml. of petroleum ether (Skellysolve "F") was added, the whole mixed well, kept in icesalt mixture for a half hour and filtered. The first and second crops of crystals were combined, p-benzoquinone (about 250 mg.) was removed by sublimation for three and a half hours at 25–45° and 0.3 mm., and the third crop was heated separately to remove p-benzoquinone to give, respectively, 2.0 4g., m. p. 133–165°, and 32 mg., m. p. 125–154°, of crude D-homosteroid (18.5%). These two fractions were combined for conversion to chrysene. Recrystallization of such material is described in a later section. Distillation of the mother liquor from the crystals gave 4.8 g. of "triene" containing a little quinone, b. p. 53–57° (0.3 mm.), and a non-volatile residue, 0.6 g. Such residues have yielded small additional quantities of adduct. The recovered "triene" no longer contains any component that will react with p-benzoquinone under the conditions employed. Similar material (3.8 g.), $n^{20}D$ 1.5283, 2.4 g. of freshly sublimed quinone, and 10 ml. of benzene were heated as described before. The only product was 100 mg. of greenish-black solid. The "triene" (2.9 g.) was recovered substantially unchanged ($n^{20}D$ 1.5284). The ultraviolet absorption characteristics of this recovered "triene" were described in the preceding section. Only a few variations of the procedure for addition of triene to p-benzoquinone were tried. It is better to take one-third an equivalent of p-benzoquinone (calcd. on whole "triene" mixture), as stated, than one equivalent.

10a-Methyloctahydrochrysene-1,4-diol (10-Methyl-13-chrysitane-2?,9(11)?-diene-15,18-diol)[19] (VI or isomeric diol) from the crude methylvinylnaphthitadiene-p-benzoquinone adduct.—To 2.07 g. of adduct was added 10.4 ml. of a solution prepared from 100 ml. of acetic acid, 1 ml. of concentrated hydrochloric acid, and 20 mg. of stannous chloride.[9] The mixture was heated on a steam-bath till solution was complete (about half an hour). Cooling in the refrigerator overnight, filtering, washing with acetic acid and water, and drying in vacuo gave 0.32 g., m. p. 195–204°. Water was added to the filtrate, the precipitate was filtered, washed with water, and dried; 1.72 g. Recrystallization of this second larger crop from benzene

(16) Woodward, THIS JOURNAL, **64**, 72 (1942).

(17) Booker, Evans and Gillam, J. Chem. Soc., 1453 (1940).

(18) Dimroth, Angew. Chem., **52**, 545 (1939).

(19) An extension of the nomenclature previously proposed (THIS JOURNAL, **64**, 1311 (1942)), to partly aromatic compounds.

gave 0.93 g., m. p. 195–201°; yield of material with m. p. 195–204°, 60%. A portion was recrystallized from benzene for analysis; m. p. 195–202°. Some specimens, prepared from recrystallized adduct, were found to have a higher m. p.

Anal. (M.) Calcd. for $C_{19}H_{22}O_2$: C, 80.8; H, 7.85. Found: C, 81.0; H, 7.8.

Chrysene from the Diol.—Recrystallized diol (555 mg.) in 20 ml. of ethanol was added to 400 mg. of Adams catalyst, which had been previously hydrogenated, in 20 ml. of ethanol. A cherry red layer formed in the portion of the solution next to the catalyst. After being stirred two minutes in hydrogen the solution became colorless. After twenty hours 69.1 ml. of hydrogen, equivalent to 1.4 double bonds, had been absorbed. In two other experiments, the uptake was equivalent to 1.5 double bonds. The solution was pale yellow at the end but became dark red as soon as it was exposed to air. Filtration of the catalyst, removal of the ethanol in carbon dioxide, and treatment with benzene gave some crystalline material but, in view of previous experience, purification before conversion to chrysene was omitted. In an earlier experiment, the dark colored crystals were washed with benzene and petroleum ether and a nearly white product, m. p. 183–196°, was obtained. This was not further investigated.

All of the product from the hydrogenation was taken up in benzene and ether, the solvents were evaporated, and the residue was kept in vacuo over paraffin for two days; 599 mg. Deoxygenation of this residue by the Clar procedure[20] was attempted, although the structure of the material is quite different from that of any of the compounds investigated by Clar. The 599 mg. of hydrogenated diol, 560 mg. of sodium chloride, 560 mg. of zinc dust, and 2.8 g. of slightly moist zinc chloride were melted together with stirring by bringing the external temperature to 185° in eight minutes. During the next six minutes the external temperature was raised to 280°. It was then held at 260–280° for three minutes more. Cooling, treating with 2 N hydrochloric acid, extracting with ether, washing the ether extract with 2 N hydrochloric acid, water and saturated sodium chloride solution, filtering through anhydrous sodium sulfate, and removing the ether gave 525 mg. of residue. Partial fractionation of this material was achieved by the use of ether and by sublimation at about half a millimeter pressure but no pure substance could be isolated.

The fractions were therefore combined, mixed with 2.63 g. of powdered selenium, sealed in a tube filled with carbon dioxide, and the tube was put into a nitrate–nitrite bath at 290°. The temperature was brought to 386° within one hour. After standing overnight the tube was opened to allow gaseous products to escape. During the heating, material vaporizing into the cooler part of the tube had been repeatedly returned to the heated part by application of a small flame. The tube was further held at 384–406° for thirty-two hours in periods of about six hours each. Between successive periods the tube was opened for the escape of gaseous products. After the last period of heating, pressure was no longer observed on opening the tube, although hydrogen selenide could still be detected. Exhaustive extraction of the products with ether and benzene gave 76 mg. of material, nearly all of which sublimed at a bath temperature of 90° and at a pressure of about half a millimeter. The sublimate was fractionated by washing the condensing surface with limited amounts of ether, and the part relatively insoluble in ether was recrystallized from benzene to give chrysene, m. p. 252–253°, mixture with authentic material, m. p. 255–256°. Thirteen mg. of pure chrysene was obtained. There was, in addition, about 12 mg. of less pure product, m. p. 230–238°, obtained by evaporation of the benzene mother liquor and crystallization from ethanol. No methylchrysene was isolated.

In a preliminary experiment, conducted similarly, crystalline material from the selenium dehydrogenation

(20) Clar, Ber., **72**, 1645 (1939).

was converted to the chrysene-2,4,7-trinitrofluorenone adduct,[21] m. p. 244.4°; mixture with authentic adduct (m. p. 248.8-250°), m. p. 246.4-247.6°.[22]

Fractional Crystallization of the Crude Adduct from the "Triene" Mixture and p-Benzoquinone.—The crude adduct has been separated into three isomeric crystalline products: A, pale yellow needles, m. p. 166-170° (after three days, m. p. 125-154°; after thirty-five days, m. p. 152-172°); B, m. p. 146-175°, later m. p. 132-157°; and C, m. p. 291-294° (evacuated tube). The crude adduct, after removal of p-benzoquinone by sublimation, was crystallized from acetone; 2.2 g. gave 1.2 g., m. p. 164-171°, and 0.75 g. of second and third crops. The first crop was recrystallized twice from ether to give 0.55 g. of A.

Anal. of Fraction A. Calcd. for $C_{19}H_{22}O_2$: C, 80.8; H, 7.85. Found: C, 80.9; H, 7.9.

This fraction, either before or after the change in melting range, can be converted quantitatively to the 10a-methyl-octahydrochrysenediol already described. This diol gave a yellow quinone, m. p. 166.4-172°, with chromic acid.

The second crop of crystals from acetone was recrystallized from acetone–hexane and the third crop from hexane. The products from these two operations were combined and recrystallized from ether to give four fractions, of which the second and third crops were the largest (0.38 g., m. p. 146-160°, and 0.1 g., m. p. 148-172°, respectively). Another recrystallization of the fraction of m. p. 146-160° from ether gave 0.2 g., m. p. 146-175°, of fraction B which is almost certainly not homogeneous.

Anal. of Fraction B. Calcd. for $C_{19}H_{22}O_2$: C, 80.8; H, 7.85. Found: C, 80.7; H, 7.85.

This fraction did not give any solid isomer when treated with the Fieser-Chang reagent[9] and the oil recovered after such treatment gave no yellow quinone with chromic acid.

Small quantities of adduct were always obtained which were insoluble in acetone. Forty milligrams was isolated in working up the batch being described. Material from several batches was combined (153 mg.) and crystallize from 200 ml. of anisole to give 101 mg. A portion of this was recrystallized again from anisole for analysis. Anisole was removed by washing with ether:

Anal. of Fraction C. Calcd. for $C_{19}H_{22}O_2$: C, 80.8; H, 7.85. Found: C, 80.8; H, 8.15.

Ultraviolet absorption[11]: Fraction A: λ_{max} 3510 Å., ϵ 83; λ_{min} 3230 Å., ϵ 62; inflection at 2950 Å.; short wave length maximum just out of the range of the instrument, ϵ at 2250 Å., 9900.[23] Fraction B: λ_{max} 3520 Å., ϵ 126; λ_{min} 3220 Å., ϵ 94; inflection at 3000 Å.; ϵ at 2250 Å., 8900. When the solution in ethanol was kept for two weeks and then reexamined, B had the following spectrum: λ_{max} 3510 Å., ϵ 250; λ_{min} 3220 Å., ϵ 185; λ_{max} 2900 Å., ϵ 1950; λ_{min} 2730 Å., ϵ 940; ϵ at 2250 Å., 8500. The new maximum which developed on standing is due to an increase in the proportion of diol. The inflections noted in the same region on examination of fresh solutions of A and B in ethanol are, no doubt, also due to the presence of a diol. The solid diol, m. p. 201-205°, in ethanol had λ_{max} 2920 Å., ϵ 3650; λ_{min} 2540 Å., ϵ 370. For hydroquinone in ethanol: λ_{max} 2930 Å., ϵ 2690.[24]

10a-Methyloctahydrochrysene-1,4-diol (10-Methyl-13-chrysitane-2?,9(11)?-diene-15,18-diol)[19] (VI or isomeric diol) from Fraction A (V?).—Some A was recrystallized from acetone–hexane, m. p. 169-171.6°; 151 mg. of this and 2.5 ml. of Fieser-Chang reagent[9] were mixed and let stand at room temperature for thirty minutes. Solution did not occur. Accordingly the mixture was warmed on a steam-bath for one hour. Removal of a small quantity of undissolved material, precipitation of product by the addition of water, washing with water, and drying in

(21) Orchin and Woolfolk, This Journal, **68**, 1727 (1946).
(22) We are very grateful to Dr. Orchin for sending us some 2,4,7-trinitrofluorenone and some chrysene-2,4,7-trinitrofluorenone.
(23) Compare Table I in Bastron, Davis and Butz, J. Org. Chem., **8**, 515 (1943).
(24) Schjånberg, Svensk Kemisk Tidskrift, **52**, 185 (1940).

vacuo over sulfuric acid gave 121 mg. (80%) of diol, m. p. 194-203°; recrystallized from benzene, 91 mg., m. p. 207.2-208.4°. Thus, freshly prepared A of high m. p. does not dissolve in the reagent at room temperature, but gives a high yield of diol at 90-100°.

Some fraction A, m. p. 168-170°, was kept for three days, whereupon the material altered so that the melting range became 125-154°. Forty-six milligrams of this lower melting material was mixed with 0.25 ml. of Fieser-Chang reagent and let stand at 23°. After one hour all had dissolved. After eighty minutes crystals began to separate and soon the whole was a solid mass of crystals. Letting stand in the refrigerator overnight, washing with water, and drying in vacuo at 50° gave 43 mg. (93%), m. p. 200.4-208.8°, no depression in m. p. when mixed with diol from fresh adduct. Thus the changes in A, indicated by change in melting range, must be formulated in a way consistent with this retained capacity for quantitative conversion to the diol.

Oxidation of the Diol to a Quinone, $C_{19}H_{20}O_2$.—To a suspension of 87 mg. of diol in 1 ml. of acetic acid was added drop by drop during half an hour a solution of 21 mg. of chromic anhydride in 0.08 ml. of acetic acid and 0.03 ml. of water at 25°. Precipitation of a yellow product occurred. Transfer of oxidant was completed with 0.08 ml. of acetic acid and the mixture was allowed to stand another half hour. Filtration, washing with acetic acid, then with water, and drying in vacuo over sulfuric acid gave 81 mg. of crude quinone. This was recrystallized twice from acetone; orange colored, m. p. 166.4-172°.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.4; H, 7.2. Found: C, 81.2; H, 7.3.

The quinone with sodium hydrosulfite gave a compound, m. p. 195-210°, which did not depress the m. p. of the diol taken for the oxidation. It is therefore XIII or an isomeric substituted p-benzoquinone. Since the objective in investigating the oxidation with chromic acid was the preparation of the naphthoquinone, XIV, in order to relate the part of the adduct which did not give a solid diol with the part which gave chrysene, the oxidation was carried out at 60° with twice the quantity of chromic anhydride specified above. This larger quantity (4 moles of chromic anhydride to 3 moles of $C_{19}H_{22}O_2$) is that calculated for complete conversion to XIV. The chief product under these conditions was the same as that obtained at the lower temperature with half the quantity of chromic anhydride. No other quinone could be isolated.

XIII   XIV
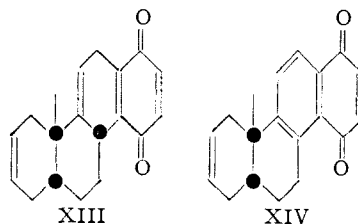
Attempt to Convert Fraction B to a Diol and a Quinone.—When 110 mg. of fraction B, m. p. 132-157°, and 0.6 ml. of Fieser-Chang reagent[9] were mixed at 31°, solution was complete in one and a half hours. After standing twenty-two hours more at room temperature, nothing had precipitated, in contrast to the behavior of fraction A. Addition of water and cooling in a refrigerator gave an oil which was washed with water and dried. This material in acetic acid was treated with 1.4 moles of chromic anhydride at 52-60° according to the procedure used for oxidation of fraction A. The aqueous filtrate did not liberate iodine from potassium iodide. Sublimation of the crude product, which was chiefly an oil, gave only 14 mg. of yellow solid, m. p. 109-129°, which could not be purified.

10a-Methyldodecahydrochrysene-1,4-dione (10-methyl-2?,9(11)?-d-homosteradiene-15,17a-dione[4] (VII).—A solution of 302 mg. of fraction A (V?), m. p. 125-154°, in 32.5 ml. of acetic acid and 10 ml. of water was added drop

by drop during twenty-five minutes with mechanical stirring to a suspension of 0.2 g. of zinc dust in 15 ml. of acetic acid and 5 ml. of water held at 52–56°. To insure a suitable distribution of zinc in the mixture, the first portion having formed into clumps, 0.2 g. more was added slowly and stirring was continued for twenty minutes with the bath at 58–60°.[10] The mixture was filtered into 100 g. of ice, the zinc was washed with a small quantity of acetic acid, the precipitated solid was removed by filtration, washed thoroughly with water, and dried *in vacuo* over sulfuric acid; slightly yellow, m. p. 120–150°, 244 mg. The filtrate was diluted with 100 ml. of water and the cloudy solution was extracted with ether. Suitable purification of the ether solution gave an oil which was united with similar material from other mother liquors, but no crystalline material was obtained from this part. Three recrystallizations of the crude solid from ether gave 62 mg. of 10-methyl-D-homosteradiene-15,17-dione, m. p. 150–163.6°, large colorless rectangular crystals.

Anal. Calcd. for $C_{19}H_{24}O_2$: C, 80.2; H, 8.5. Found: C, 80.2; H, 8.55.

An additional 82 mg., m. p. 148–167.6°, was obtained from the ether mother liquors. This was treated with 2,4-dinitrophenylhydrazine. At room temperature, inseparable mixtures of mono- and bis-hydrazones were obtained. Boiling such a mixture with twice its weight of 2,4-dinitrophenylhydrazine in ethanol for a half hour, filtration,

washing with 2 N hydrochloric acid and water, boiling with ethyl acetate, and recrystallizing, first from anisole and then from benzene, gave the **bis-2,4-dinitrophenylhydrazone**; 257–260° (dec.).

Anal. Calcd. for $C_{31}H_{32}N_8O_8$: N, 17.4. Found: N, 17.5.

Summary

1. A 1-ethynyl-10-methylnaphthiten-1-ol has been hydrogenated to a 10-methyl-1-vinylnaphthiten-1-ol which was dehydrated to a mixture of hydrocarbons.

2. Reaction with *p*-benzoquinone demonstrated the presence of the 1-vinyl-1-naphthitene group in one of the components of the mixture, since the product of the reaction was converted to chrysene.

3. This product was isomerized to an octahydrochrysene-*ar*-1,4-diol and reduced to a 10-methyl-D-homosteradiene-15,17a-dione in which one C=C bond is probably in ring A and the other in ring C.

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p-Alkoxybenzenesulfonic Acid Esters

BY MARIE H. CARR[1] AND HAROLD P. BROWN

Unsuccessful attempts[1a] to prepare the sulfur analog of the local anesthetic procaine, the diethylaminoethyl ester of *p*-aminobenzoic acid, have been reported in the literature. Because of the recognized chemotherapeutic value of many sulfur compounds the syntheses of the sulfur analogs of another group of efficient local anesthetics,[2,3,4,5] namely, the *p*-alkoxybenzoic acid esters, was undertaken. Using sodium *p*-hydroxybenzenesulfonate as a starting material, the methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, β-chloroethyl and β-bromoethyl esters of *p*-methoxy, *p*-ethoxy, *p*-*n*-propoxy and *p*-*n*-butoxybenzenesulfonic acids were prepared. Attempts to prepare the β-diethylaminoethyl esters were not successful. The syntheses were accomplished by (1) etherification of the *p*-hydroxy group, (2) conversion of the sodium salt to the sulfonyl chloride, and (3) esterification by the appropriate alcohol. Solubilities in water and organic solvents, melting points, boiling points, sulfur content, saponification equivalents, and preliminary indications of physiological activity were determined.

(1) Condensed from a thesis submitted to the Faculty of the Department of Chemistry of the University of Kansas City in partial fulfillment of the requirements for the degree of Master of Arts.

(1a) G. E. Crossen, G. L. Jenkins and C. E. Rogers, *Pharm. Arch.*, **12**, 21 (1941).

(2) C. Rohmann and B. Scheurle, *Arch. Pharm.*, **274**, 110 (1936).

(3) C. Rohmann and K. Friedrick, *Ber.*, **72B**, 1333 (1939).

(4) C. Rohmann and A. Koch, *Arch. Pharm.*, **276**, 154 (1938).

(5) W. A. Lott, S. E. Harris and W. G. Christiansen, *J. Am. Pharm. Assoc.*, **27**, 661 (1938).

Experimental

A.   *p*-Alkoxybenzenesulfonic Acids.—The method recommended by Fieser[6] for the preparation of aryl-alkyl ethers was found satisfactory and produced good yields. The following modified procedures were adopted:

Sodium *p*-Methoxybenzenesulfonate.—To 120 g. of sodium *p*-hydroxybenzenesulfonate dissolved in 200 ml. of 15% sodium hydroxide, were added 100 ml. of methanol and 80 ml. of methyl sulfate. With the mouth of the flask partially closed by a funnel, the mixture was heated on a water-bath for one hour, chilled thoroughly, and the resulting fine white crystals filtered off. The sodium *p*-methoxybenzenesulfonate was washed with small quantities of ice water, then dried. An average yield of 75% was obtained.

Sodium *p*-Ethoxybenzenesulfonate.—This compound was prepared in essentially the same manner, using 90 ml. of ethyl sulfate. As ethanol did not increase the yield of ethoxysulfonate, it was omitted and replaced by 100 ml. of water. The average yield was 73%.

Sodium *p*-*n*-Propoxybenzenesulfonate.—*n*-Propyl bromide and ethanol were used in this synthesis. The reaction mixture was refluxed fifteen to eighteen hours according to the procedure of Hartley.[7] A yield of 68% was obtained.

Sodium *p*-*n*-Butoxybenzenesulfonate.—This compound was prepared in the same manner as the propoxy, using 70 ml. of *n*-butyl bromide. The yield was 65%.

The sodium *p*-alkoxybenzenesulfonates were all white crystalline compounds, very soluble in water and hot alcohol, insoluble in acetone, ether, chloroform, benzene, and ligroin. On heating, they charred without melting.

B.   *p*-Alkoxybenzenesulfonyl Chlorides.—The sodium *p*-alkoxybenzenesulfonates were readily converted to the sulfonyl chlorides by heating equal quantities of the well

(6) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Company, New York, N. Y., 1941, p. 374.

(7) G. Spencer Hartley, *J. Chem. Soc.*, 1828 (1939).