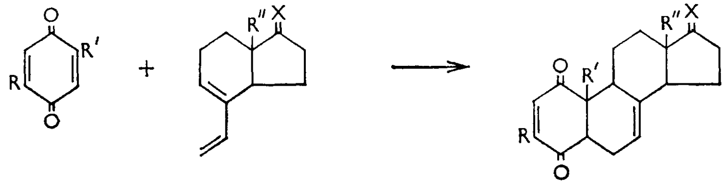
773. *The Addition of* p-*Benzoquinones to* 2,3,3*a*,4,5,7*a*-*Hexahydro*-7-*vinylindene.*

By Angel Alberola, M. Lora-Tamayo, José L. Soto, and M. Soto.

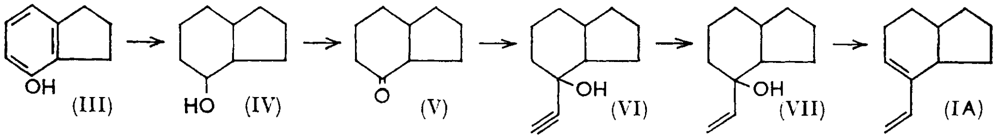
The Diels–Alder reactions of 2,3,3a,4,5,7a-hexahydro-7-vinylindene with *p*-benzoquinone, toluquinone, and methoxy-*p*-benzoquinone are reported. In each case the product contained a hydrocyclopenta[*a*]phenanthrene nucleus; when a monosubstituted quinone was used the substituent appeared at position 3 of the adduct. The preparation of the 2,3,3a,4,5,7a-hexahydro-7-vinylindene is described.

With the object of obtaining hydrocyclopenta[*a*]phenanthrene derivatives of potential biological interest we have studied the addition of dienes (I) related to substituted *p*-benzoquinones, whereby the diene affords rings C and D of a possible steroid. In this paper we record work only on 2,3,3a,4,5,7a-hexahydro-7-vinylindene itself (I; $R'' = H, X = H_2$). Although five asymmetric centres (5, 9, 10, 13, and 14) are formed in the reaction the configurations at all of these are determined by that of initial diene and by the stereochemical requirements of the Diels–Alder reaction. On the other hand, the oxo-groups at positions 1 and 4 may lead to inversion of the adjacent asymmetric carbon atoms, giving the possibility of transformation into the natural steroid system.



I (A; $R'' = H, X = H_2$) (II)

As data on dienes of type (I) were not available, we synthesised 2,3,3a,4,5,7a-hexahydro-7-vinylindene (IA). Hydrogenation of indan-4-ol (III) at 150°/150 atm. with Raney nickel as catalyst led to perhydroinden-4-ol[1] (IV) and thence by oxidation by chromic acid to the ketone (V).[2,3] Reaction of this ketone with potassium acetylide in liquid ammonia yielded 4-ethynylperhydroinden-4-ol (VI), which on hydrogenation in presence of quinoline-poisoned palladium gave 4-vinylperhydroinden-4-ol (VII). Dehydration to 2,3,3a,4,5,7a-hexahydro-7-vinylindene (IA) was achieved by heating the alcohol with potassium hydrogen sulphate in an inert atmosphere. It was difficult to obtain pure specimens of this hydrocarbon but repeated fractionations at reduced pressure gave almost pure diene.



2,3,3a,4,5,7a-Hexahydro-7-vinylindene (IA) with maleic anhydride in benzene gives the adduct (VIII). With *p*-benzoquinone in the same solvent it gives the *syn*-*cis*-dodecahydrocyclopenta[*a*]phenanthrene dione (IX).* The ultraviolet spectrum of this has a main

---

* Compounds obtained are racemic although only one enantiomer is illustrated. The 13,14-ring junction is *trans* but its relation to the other asymmetric centres is unknown.

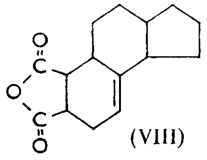
[1] Hückel, *Annalen*, 1937, **533**, 128.

[2] Hückel and Goth, *Ber.*, 1934, **67**, 2104.

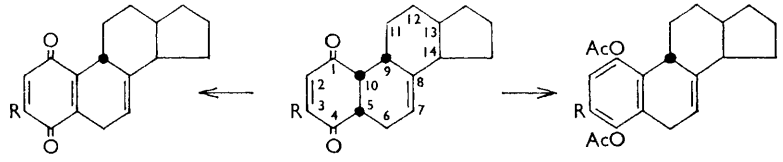
[3] Bachmann and Struve, *J. Amer. Chem. Soc.*, 1941, **63**, 2589.

band at 227 mμ (log ε 4·01) and a secondary band at 292 mμ (log ε 2·20), both characteristic of the chromophore system CO·CH:CH·CO; [4] an infrared peak at 1697 cm.$^{-1}$ corresponds to $\alpha\beta$-unsaturated ketone groups. When the diketone (IX) is treated with acetic anhydride the corresponding diacetyl derivative (X) is obtained.

The *syn-cis*-configuration of the A and B nuclei is established by Alder's [5] rules. In accordance with them Robins and Walker,[4] among others, assign these configurations to the products of the reactions of 1-vinylcyclohexene and 1,2-dihydro-7-methoxy-4-vinylnaphthalene with *p*-benzoquinone, and Woodward *et al.*[6] assign a *cis*-configuration to the butadiene–4-methoxytoluquinone adduct to which Orchin and Butz [7] previously assigned a *trans*-configuration. The fact that the diketone (IX) is the only identifiable product obtained in the reaction corroborates this assignment, as in diene syntheses where these rules are, apparently, not followed, stereoisomeric mixtures are obtained.[8]



(VIII)



(XIII: R = OMe)
(XVI: R = Me)

(IX: R = H)
(XI: R = OMe)
(XIV: R = Me)

(X: R = H)
(XII: R = OMe)
(XV: R = Me)

We next studied additions that might lead closer to steroids. Addition of methoxy-*p*-benzoquinone to the diene (IA) occurred with a high degree of selectivity, yielding only one compound (XI), whose structure was elucidated by chemical and spectroscopical methods. Its ultraviolet spectrum (Fig. 1) shows maximum absorption at 274 mμ (log ε 3·96), characteristic of the chromophore system CO·CH:C(OMe)·CO; [6,9] infrared bands at 1683 and 1605 cm.$^{-1}$ are due, respectively, to the $\alpha\beta$-unsaturated diketone grouping and to the conjugated double bond. With acetic anhydride the product yields a diacetate (XII), whose ultraviolet absorption (Fig. 2) agrees with that of 2,5-diacetoxyanisole and shows that condensation has taken place on the unsubstituted double bond of the quinone. The configurations of the asymmetric centres C-5, C-9, and C-10 are established by Alder's rules. The position of the methoxyl group was demonstrated by the following reactions: Lithium aluminium hydride reduced the adduct to the methoxy-diol (XVII) which, on dehydration by potassium hydrogen sulphate followed by dehydrogenation over palladium gave the known compound (XVIII), m. p. 134—136° (lit.,[10] 136—137°). Sulphuric acid hydrolyses the diol (XVII) with partial dehydration, to give the hydroxy-ketone (XIX) which is of special interest in relation to steroids.

On chromatography on alumina in benzene the diol (XI) is transformed into the quinone (XIII), which by reductive acetylation gives a quinol diacetate (XII).

Compound (XIV) is the only product obtained in the reaction of the diene (IA) with toluquinone. Its ultraviolet spectrum (Fig. 1) shows the presence of the chromophore CO·CH:CMe·CO.[4] This compound yields a diacetate (XV) on reaction with acetic

---

[4] Ansell and Culling, *J.*, 1961, 2908; Robins and Walker, *J.*, 1952, 642, 1610; 1956, 3294.

[5] Alder and Stein, *Angew. Chem.*, 1937, **50**, 510; Bergmann and Eschinazi, *J. Amer. Chem. Soc.*, 1943, **65**, 1405.

[6] Woodward, Sondheimer, Taub, Heusler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223.

[7] Orchin and Butz, *J. Org. Chem.*, 1943, **8**, 509.

[8] Lukes, Poos, and Sarett, *J. Amer. Chem. Soc.*, 1952, **74**, 1402; Alberola, Lora-Tamayo, del Rey, and Soto, *Anales real Soc. esp. Fis. Quim.*, in the press.

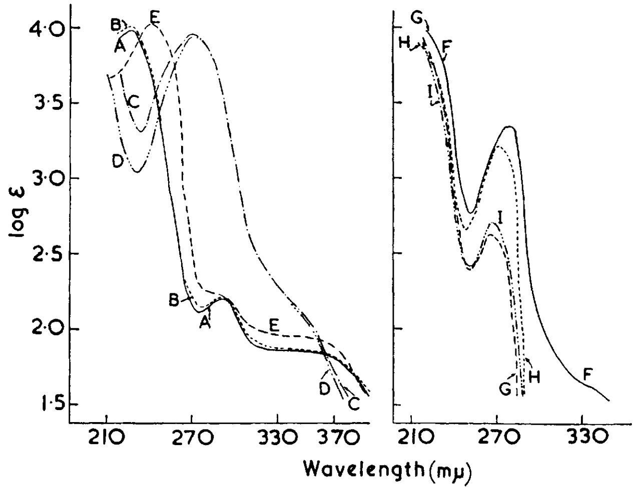
[9] Ansell and Knights, *J.*, 1961, 2903.

[10] Cohen, Cook, Hewett, and Girard, *J.*, 1934, 653.

anhydride, whose structure follows from the relation of its ultraviolet spectrum (Fig. 2) to that of 2,5-diacetoxytoluene (Fig. 2).

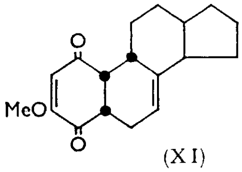
Prolonged boiling of an ethanol solution of the diketone (XIV) yields a strongly coloured product, shown to have structure (XVI) by its lack of reactivity with acetic anhydride, its transformation into the diacetate (XV) by reductive acetylation, and by the 1657 cm.$^{-1}$ band in its infrared absorption spectrum.

FIG. 1 FIG. 2

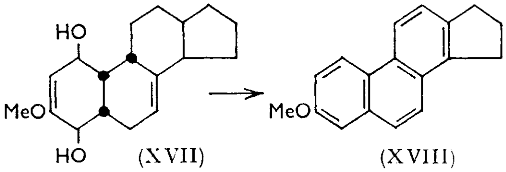


Ultraviolet absorption of: (FIG. 1) (A) compound (XI), (B) *cis-syn*-1,4,4a,4b,5,6,7,8,10,10a-decahydrophenanthrene-1,4-dione, (C) compound (XI), (D) the 2-methoxy-derivative analogous to (B), and (E) compound (XIV); (FIG. 2.) (F) compound (XII), (G) compound (XV), (H) methoxyquinol diacetate, and (I) toluquinol diacetate.

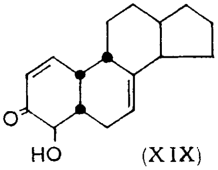
In the reaction of the hexahydroindene (IA) with methoxytoluquinone, which could yield adducts with an angular methyl group, only poorly defined, unidentified, irreproducible products were obtained.



(XI)



(XVII) (XVIII)



(XIX)

EXPERIMENTAL

Infrared spectra were recorded with a Perkin–Elmer model 112 spectrograph with sodium chloride prism. Ultraviolet spectra were measured for anhydrous ethanol solutions with a Beckman DU spectrophotometer.

Perhydroinden-4-ol (IV).—Indan-4-ol (100 g.) and Raney nickel (30 g.) in anhydrous methanol (250 ml.) were heated in a stainless-steel oscillating autoclave at 150° for 6 hr. under hydrogen at 150 atm. The mixture was then filtered and evaporated, and the residue fractionated at reduced pressure to yield perhydroinden-4-ol (98 g.), b. p. 104—106°/12 mm. The *p*-nitrobenzoate, crystallised from ethanol, had m. p. 72° (lit.,[2] 72°).

Perhydroinden-4-one.—The ketone [2] gave a 2,4-*dinitrophenylhydrazone*, red needles (from ethanol), m. p. 155° (Found: C, 57·0; H, 5·9; N, 17·2. $C_{15}H_{18}N_4O_4$ requires C, 56·6; H, 5·7; N, 17·6%).

4-*Ethynylperhydroinden*-4-*ol* (VI).—Potassium (12 g.) was dissolved in liquid ammonia (500 ml.) containing ferric nitrate (0·1 g.) by 1 hour's stirring at −50°. Acetylene, washed by passage through concentrated sulphuric acid, was passed into the solution for 2 hr., affording potassium acetylide. Then perhydroinden-4-one (38 g.) in ether (50 ml.) was added and stirring continued for 4 hr. The grey colour changed to light yellow and a dark precipitate appeared. The temperature was then allowed to rise to −30° and ammonium chloride (20·3 g.) was added in portions. The whole was left overnight at room temperature, most of the ammonia evaporating. The residue was dissolved in ether (300 ml.) and water (200 ml.), and the aqueous layer was extracted with ether (2 × 150 ml.). The ethereal solutions were combined and concentrated to 250 ml., then dried (Na_2SO_4) and evaporated. The residue was distilled, giving the 4-*ethynylperhydroinden*-4-*ol* (42·4 g., 94%), b. p. 107—110°/13 mm., m. p. 62—64° (from ligroin), $\nu_{max.}$ 3744 and 3405 (OH), 3307 and 2106 cm.$^{-1}$ (C≡C group) (Found: C, 80·4; H, 10·0. $C_{11}H_{16}O$ requires C, 80·5; H, 9·75%). Its p-*nitrobenzoate* had m. p. 112—114° (from aqueous ethanol) (Found: C, 69·0; H, 6·0; N, 4·4. $C_{18}H_{19}NO_4$ requires C, 69·0; H, 6·1; N, 4·5%).

Perhydro-4-*vinylinden*-4-*ol* (VII).—The acetylenic alcohol (63 g.) in ethyl acetate (580 ml.) was hydrogenated at 1 atm. in presence of 5% palladium–charcoal (6·3 g.) and quinoline (6·3 g.) until 8·6 l. of hydrogen had been absorbed. After filtration and evaporation (water pump), the residue was dissolved in ether and washed with 5% hydrochloric acid, 5% sodium hydrogen carbonate solution, and water. After drying (Na_2SO_4) the solvent was removed on a water-bath. Distillation of the residue gave *perhydro*-4-*vinylinden*-4-*ol* (60·2 g.), b. p. 105—108°/13 mm., n_D^{23} 1·4996, $\nu_{max.}$ 3744 and 3431 (OH), 3110, 992, and 920 cm.$^{-1}$ (C=C) (Found: C, 79·3; H, 10·9. $C_{11}H_{18}O$ requires C, 79·5; H, 10·8%). The 3,5-*dinitrobenzoate* separated from aqueous ethanol as yellow needles, m. p. 106—107° (Found: C, 60·2; H, 5·5; N, 7·8. $C_{18}H_{20}N_2O_6$ requires C, 60·0; H, 5·55; N, 7·8%).

2,3,3a,4,5,7a-*Hexahydro*-7-*vinylindene* (IA).—The alcohol (VIII) (18 g.) was heated with fused potassium hydrogen sulphate (9 g.) under nitrogen at 125—135°/36 mm. The first hydrocarbon fractions co-distilled at 45—50° with the water formed in the reaction; then the *diene* distilled at 110—115°. This product was dissolved in ether and dried (Na_2SO_4) and the solvent was removed in a vacuum. The residue was fractionated in an inert atmosphere in the presence of quinol, yielding a liquid (13·2 g., 84%), b. p. 92—94°/12 mm., which rapidly became yellow, $\lambda_{max.}$ 232 mμ (log ε 4·03) (Found: C, 88·9; H, 11·3. $C_{11}H_{16}$ requires C, 89·2; H, 10·8%).

Reaction of the Diene (IA) *with Maleic Anhydride*.—The diene (7·7 g., 0·053 mole) was heated with maleic anhydride (5·1 g., 0·052 mole) in benzene (30 ml.) for 6 hr. The solvent was distilled off under a vacuum and the remaining solid washed with water (30 ml.). Crystallisation from light petroleum gave 2,3,3a,4,5,5a,6,7,8,9b-*decahydro*-1H-*benz*[e]*indene*-6,7-*dicarboxylic anhydride* (VIII) (2 g.) as plates, m. p. 156—158° (Found: C, 72·9; H, 7·1. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·3%).

Reaction of the Diene (IA) *with Quinones*.—The diene and dienophile (molar ratio 1 : 1) in anhydrous benzene were heated under reflux for 48 hr. The solution was then filtered, the solvent driven off at reduced pressure, and the residue washed with a small amount of cold ethanol and crystallised from the same solvent. The adducts obtained formed white or yellowish-white crystals, as follows:

cis-syn-$\Delta^{2,7}$-*Dodecahydro*-15H-*cyclopenta*[a]*phenanthrene*-1,4-*dione* (IX), needles, m. p. 122°, $\lambda_{max.}$ 227, 292 mμ (log ε 4·01, 2·20) (Found: C, 79·6; H, 8·0. $C_{17}H_{20}O_2$ requires C, 79·6; H, 7·8%).

cis-syn-$\Delta^{2,7}$-*Dodecahydro*-3-*methoxy*-15H-*cyclopenta*[a]*phenanthrene*-1,4-*dione* (XI), needles, m. p. 200°, $\lambda_{max.}$ 274 mμ (log ε 3·96) (Found: C, 75·3; H, 7·9. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·7%).

cis-syn-$\Delta^{2,7}$-*Dodecahydro*-3(or 2)-*methyl*-15H-*cyclopenta*[a]*phenanthrene*-1,4-*dione* (XIV), needles, m. p. 165°, $\lambda_{max.}$ 245 mμ (log ε 4·02) (Found: C, 80·2; H, 8·3. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·1%).

Acetylation of the Adducts.—The adduct (0·5 g.), acetic anhydride (10 ml.), anhydrous sodium acetate (0·12 g.) were heated under reflux for 1 hr., cooled, poured into water, and stirred to decompose the anhydride. The solid was filtered off, washed with water, and crystallised from ethanol or aqueous ethanol, affording cis-syn-1,4-*Diacetoxy*-6,9,11,12,13,14,16,17-*octahydro*-15H-*cyclopenta*[a]*phenanthrene* (X), needles, m. p. 84° (Found: C, 74·0; H, 7·4.

$C_{21}H_{24}O_4$ requires C, 74·1; H, 7·1%), and its 3-*methoxy*- (XII), needles, m. p. 139°, $\lambda_{max.}$ 280 mμ (log ε 3·36) (Found: C, 71·1; H, 6·9. $C_{22}H_{26}O_5$ requires C, 71·3; H, 7·0%), and 3(or 2)-*methyl derivative* (XV), needles, m. p. 133°, $\lambda_{max.}$ 266 mμ (log ε 2·62) (Found: C, 74·2; H, 7·2. $C_{22}H_{26}O_4$ requires C, 74·5; H, 7·3%).

Conversion of the Adduct (XI) *into the Quinone* (XIII).—The adduct in benzene was chromatographed on Merck alumina, with benzene as eluent. Removal of the solvent at reduced pressure gave a quantitative yield of 1,4,6,9,11,12,13,14,16,17-*decahydro*-15H-*cyclopenta*[a]*phenanthrene*-1,4-*dione* (XIII) which crystallises from ethanol in yellow needles, m. p. 152—154° (Found: C, 75·8; H, 6·6. $C_{18}H_{20}O_3$ requires C, 76·0; H, 7·0%).

Oxidation of the Adduct (XIV) *to the Quinone* (XVI).—The adduct (2 g.) in solution in ethanol was heated under reflux for 5 hr., the colour changing from pale yellow to dark blue. The volume was reduced to one-half; then crystallisation gave 1,4,6,9,11,12,13,14,16,17-*decahydro*-2(or 3)-*methyl*-15H-*cyclopenta*[a]*phenanthrene*-1,4-*dione* (XVI) as brown needles, m. p. 177—178°. The change is accelerated by a few drops of hydrogen peroxide (Found: C, 80·3; H, 7·7. $C_{18}H_{20}O_2$ requires C, 80·0; H, 7·5%).

Acetylating Reduction of the Quinones.—To the quinone (0·5 g.), acetic anhydride (10 ml.), acetic acid (2 ml.), and sodium acetate (0·12 g.), heated under reflux, zinc dust (0·5 g.) was added during 1 hr. Heating was continued for a further hr. and the solution left to cool and then poured into water with stirring. The diacetoxy-compound was filtered off and crystallised from ethanol. The reaction with the quinones (XIII) and (XVI) yielded compounds (XII) and (XV).

cis-syn-$\Delta^{2,7}$-*Dodecahydro*-3-*methoxy*-15H-*cyclopenta*[a]*phenanthrene*-1,4-*diol* (XVII).—The methoxy-diketone (XI) (5·5 g.) in tetrahydrofuran (400 ml.) and ether (300 ml.) was added under nitrogen to lithium aluminium hydride (3·8 g.) in ether (30 ml.) and the whole heated under reflux on the water-bath for 5 hr., then cooled and treated successively with ethyl acetate (25 ml.), sodium sulphate solution, and magnesium sulphate (11 g.). After short further stirring the solution was filtered and the solids were washed with ether. Evaporation of the combined filtrates gave a residue which crystallised from benzene to afford the *diol* (2 g.), m. p. 174° (decomp.) (Found: C, 74·5; H, 9·2. $C_{18}H_{26}O_3$ requires C, 74·4; H, 9·0%).

3-*Methoxycyclopenta*[a]*phenanthrene* (XVIII).—The diol (XVII) (1·3 g.) and fused potassium hydrogen sulphate (2·6 g.) were heated at 180° for 45 min. under nitrogen. The resulting mass was stirred with water and extracted several times with ether. The extracts were washed with sodium hydrogen carbonate solution and dried ($CaCl_2$). The solvent was distilled off. Addition of ether (5 ml.) to the oily residue yielded a yellowish solid (1 g.). This was heated for 3 hr. at 300° in a carbon dioxide atmosphere in the presence of 0·75 g. of 5% palladium–charcoal. The product was extracted with benzene; evaporation of this extract gave a residue which was extracted with boiling ethanol; evaporation of the alcohol solution gave a yellowish solid which was chromatographed in ligroin (b. p. 50—70°) on alumina with the same solvent as eluent. Removal of the ligroin yielded the hydrocarbon (XVIII) (0·2 g.), m. p. 134—136° (corr.) (from ethanol) [lit.,[10] 136—137° (corr.)] (Found: C, 87·4; H, 6·5. $C_{18}H_{16}O$ requires C, 87·1; H, 6·5%). The 1,3,5-trinitrobenzene complex separated from ethanol as orange needles, m. p. 161—165° (corr.) [lit.,[10] 161—165° (corr.)].

cis-syn-$\Delta^{1,7}$-*Dodecahydro*-4-*hydroxy*-15H-*cyclopenta*[a]*phenanthren*-3-*one* (XIX).—The diol (XVII) (13 g.) and 2N-sulphuric acid (50 ml.) in dioxan (1·2 l.) were set aside for 24 hr. at room temperature with occasional stirring. Then the solution was poured into much water, left overnight at 0°, and extracted several times with ether. The combined extracts were washed with sodium hydrogen carbonate solution and with water, dried (Na_2SO_4), and evaporated. The residual *hydroxy-ketone* (XIX), when crystallised from ligroin, had m. p. 158—160° (Found: C, 79·3; H, 8·45. $C_{17}H_{22}O_2$ requires C, 79·1; H, 8·5%).

The authors are indebted to Juan March Foundation for a fellowship (to M. S.).

" ALONSO BARBA " INSTITUTE OF CHEMISTRY,
SERRANO 119, MADRID 6, SPAIN.

[*Received, February* 28*th*, 1962.]