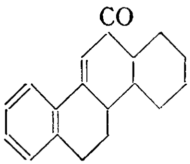
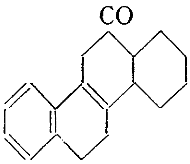
174. *Experiments on the Synthesis of Substances Related to the Sterols. Part XII. Some Hydrochrysene Derivatives.*

By D. A. PEAK and ROBERT ROBINSON.

THE condensation of sodio-α-tetralone with acetyl*cyclo*hexene under conditions similar to those prescribed in Part II (Rapson and Robinson, J., 1935, 1285) proceeds unusually smoothly and a *ketodecahydrochrysene-A* (I) is obtained in yields up to 80%. This substance has therefore been examined in detail. The mother-liquors from the first preparation of (A) afforded an isomeride (B), and a third isomeride (C) was isolated in a similar way in subsequent experiments. The substances (A), (B), and (C) are undoubtedly distinct chemical individuals and not mixtures; their melting points are widely separated and mixtures showed large depressions.


(I.)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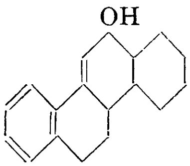
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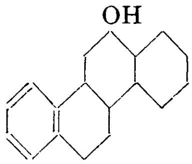

(IV.)

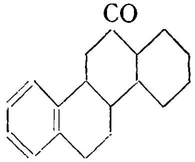
Mr. A. E. Gillam of the Chemistry Department of the University of Manchester has kindly reported on the absorption spectra of these isomerides. (A) and (B) show identical absorption, which is similar to that characteristic of benzylideneacetone; (C) gives entirely different results indicating that the unsaturated group is no longer conjugated with the carbonyl. Hence (A) and (B) are stereoisomerides (I) and the formula (II) is the best that can be attributed to (C). Unfortunately the isomerides (B) and (C) were accessible in such small quantities that their transformations could not be fully examined.

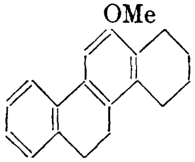
An attempt to convert (A) into (C) was made by refluxing the substance with alcoholic sodium ethoxide, but the outcome was remarkable because the product was the unsaturated *alcohol* (III), which yields a *phenylurethane*. A parallel for this reaction in a very different region of organic chemistry may be found in the reduction of diacetyldeuteroporphyrin (Fischer and Zeile, *Annalen*, 1929, **468**, 98). Catalytic reduction of (I)-A yields a *hydroxydodecahydrochrysene-α* (IV), and an isomeride (β) is produced when reduction is effected by means of sodium and alcohol. In this case the isomerism is concerned with the configuration of the *sec.*-alcohol group and isomeride-α can be converted into the β-form by treatment with *iso*amyl-alcoholic sodium *iso*amyloxide.

On oxidation with chromic acid the α- and the β-form gave one and the same *ketone* (V). This substance could not be converted into a benzylidene derivative, doubtless as the result of real steric hindrance.

An attempt to methylate the ketone by means of sodamide and methyl iodide was fruitless, but when the unsaturated ketone (I)-A was similarly treated a methoxyl-containing compound, probably (VI), was obtained.

(V.)





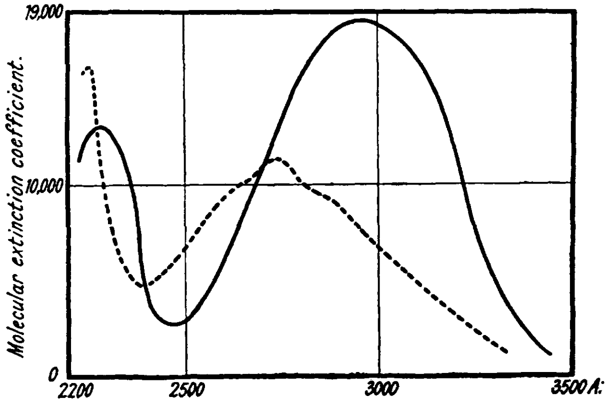
(VI.)

The Clemmensen reduction of (I)-A furnished a decahydrochrysene which was doubtless a mixture, whereas a homogeneous *decahydrochrysene* was obtained by applying the Wolff–Kishner method to the saturated ketone (V). This decahydrochrysene gave chrysene when it was heated with selenium at 310—320°.

Finally it is interesting that the unsaturated ketone (I)-A also afforded chrysene when it was heated with selenium. A by-product of this reaction was a *substance*, $C_{18}H_{12}O$. This reduction of a carbonyl group in a selenium dehydrogenation process is not unique; it has been observed in the phenanthrene series and is perhaps due to the powerful reducing properties of the intermediate products of the dehydrogenation.

EXPERIMENTAL.

2-*Keto*-2 : 3 : 4 : 5 : 6 : 7 : 8 : 14 : 15 : 16-*decahydrochrysene-A* (I).—Sodio-α-tetralone was prepared from α-tetralone (15·7 g.) (Hock and Susemihl, *Ber.*, **1933**, **66**, 61) and finely powdered sodamide (4·2 g.) in anhydrous ether (200 c.c.) with stirring at room temperature for 7 hours, ammonia being removed in a stream of dry oxygen-free nitrogen, and finally by gentle refluxing for 1 hour. Acetyl*cyclo*hexene (13·3 g.) (Ruzicka, Koolhaas, and Wind, *Helv. Chim. Acta*, **1931**, **14**, 1157), dissolved in ether (20 c.c.), was then added drop-wise with stirring and ice-cooling. After 12 hours the crystalline mass which had separated was collected after addition of dilute sulphuric acid and washed with alcohol and ether. The crude *product* (19·0 g.; 70% yield) after one recrystallisation from ethyl alcohol (1000 c.c.) was pure. It separated from this solvent in glistening needles, m. p. 200—200·5° (Found: C, 85·5; H, 7·9. $C_{18}H_{20}O$ requires C, 85·7; H, 7·9%), or from dilute solutions in large square plates which on recrystallisation reverted to the needle form. Both forms appeared stable, no interchange being observed when mixtures of the crystals were left for several weeks in contact with alcohol. The substance was sparingly soluble in all solvents except hot alcohol, ethyl acetate, and acetone.



Ketodecahydrochrysenes : ——— *Isomerides A and B.*
------ *Isomeride C.*

In subsequent condensations by refluxing the reaction mixture for 2 hours after the initial reaction at room temperature for 12 hours, the yield was as high as 80%.

2-*Keto*-2 : 3 : 4 : 5 : 6 : 7 : 8 : 14 : 15 : 16-*decahydrochrysene*-*B* (I).—In the initial condensation, the ethereal solution on concentration deposited a second substance (0·9 g.) more readily soluble in all solvents than the first substance. It was recrystallised several times from alcohol, separating in fine needles, m. p. 152—153° (Found : C, 85·8; H, 8·0%). The m. p. was much depressed on admixture with the isomeride A.

2-*Keto*-1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 15 : 16-*decahydrochrysene*-*C* (II).—Subsequent condensations yielded none of the isomeride B. The residue after complete removal of the ether gave a small fraction, b. p. 190—210°/2 mm., which partly crystallised in contact with ether. It was recrystallised several times from ethyl alcohol, aqueous methyl alcohol, and aqueous acetone, separating in small needles, m. p. 115—115·5° (Found : C, 86·0; H, 8·2%). The substance was more readily soluble in all solvents than isomerides A and B and its m. p. was considerably depressed by addition of either of the latter.

Substance.	Absorption spectrum.	Molecular extinction coefficient, ε.
A	One broad band, max. 2960 A. (min. 2460 A.) and a second indefinite band at 2290 A.	18,650
B	,, ,, ,,	18,650
Benzylideneacetone.	One broad band, max. 2850 A.	23,000
Phenyl styryl ketone	One band at 3100 A., min. 2460 A.	26,000
C	Broad band with incipient narrow bands on either side of main maximum.	10,600
	Inflexion, 2640 A. Main max., 2750 ,, Inflexion, 2860 ,, 1 minimum, 2390 ,,	10,600

Attempted Methylation of 2-*Ketodecahydrochrysene*-*A*. *Isolation of* 2-*Methoxy*-3 : 4 : 5 : 6 : 7 : 8-*hexahydrochrysene* (VI ?)—The sodio-derivative of the unsaturated ketone (3·1 g.) was formed by refluxing it with sodamide (0·5 g.; 1 mol.) in dioxan (100 c.c.), previously distilled from sodium and sodamide, until evolution of ammonia had ceased (3 hours). Methyl iodide (3·5 g.; 2 mols.) was then added, and refluxing continued until the solution was neutral to moist litmus (3 hours). The filtered solution was concentrated to 10 c.c. and yielded unchanged material (0·6 g.) together with an uncrystallised residue, b. p. 190—200°/3 mm. The distillate partly crystallised in contact with ether, yielding further unchanged material (0·4 g.). The residue then gradually crystallised from aqueous alcohol, yielding a *substance* (0·25 g.) which, recrystallised from ethyl or methyl alcohol, gave well-formed long plates, m. p. 95·5—96° (Found : C, 86·2; H, 7·4; OMe, 10·8, 10·8. $C_{19}H_{20}O$ requires C, 86·4; H, 7·6; OMe, 11·7%).

2-*Hydroxy*-2 : 3 : 4 : 5 : 6 : 7 : 8 : 14 : 15 : 16-*decahydrochrysene*.—2-Ketodecahydrochrysene-A (3 g.) was refluxed with a solution of sodium (5 g.) in absolute alcohol (50 c.c.) for 7 hours. The deep red liquid was mixed with water and extracted with ether. The residue after removal of the ether had b. p. 216—218°/3 mm. The light yellow, vitreous mass (1·9 g.) crystallised in contact with ether and then separated from 50% aqueous ethyl alcohol in small colourless needles, m. p. 136° (Found : C, 85·0; H, 8·7. $C_{18}H_{22}O$ requires C, 85·0; H, 8·7%). The *substance* was extremely soluble in the usual organic solvents. Its *phenylurethane* crystallised from ethyl alcohol in needles, m. p. 173—173·5° (Found : C, 80·4; H, 7·3. $C_{25}H_{27}O_2N$ requires C, 80·4; H, 7·3%).

2-*Hydroxy*-1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 13 : 14 : 15 : 16-*dodecahydrochrysene*-α (IV).—The unsaturated ketone (I)-A (9·9 g.) was hydrogenated in ethyl-alcoholic suspension (250 c.c.) by shaking with a 2% palladium–strontium carbonate catalyst (3 g.) for 10 hours in hydrogen at 3 atm. pressure. The catalyst along with unchanged material (1·0 g.) was collected; the filtrate on concentration to 10 c.c. slowly deposited crystals (4·0 g.), which separated from aqueous ethyl alcohol in fine needles, m. p. 114—115° (Found : C, 84·3; H, 9·1. $C_{18}H_{24}O$ requires C, 84·4; H, 9·4%). Further quantities of less pure material slowly separated from the mother-liquors. The *substance* was freely soluble in most organic solvents. The *phenylurethane* separated from alcohol in clusters of needles, m. p. 197—198° (Found : N, 3·6. $C_{25}H_{29}O_2N$ requires N, 3·7%).

When ethyl acetate was used as the solvent in this hydrogenation process, the main product was the *saturated* ketone (*q.v.*).

2-*Hydroxy*-1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 13 : 14 : 15 : 16-*dodecahydrochrysene*-β (IV).—(1) The unsaturated ketone (I)-A (5·0 g.) was dissolved in hot absolute alcohol (250 c.c.), and a large excess of sodium (25 g.) added in small pieces to the boiling solution. The alcohol was then removed under diminished pressure, and the residual solid decomposed with water (500 c.c.). The warm clear solution on cooling deposited clusters of needles (2·3 g.), which crystallised from 30% aqueous alcohol in fine small needles, m. p. 134—135° (Found : C, 84·3; H, 9·3%). The material was easily soluble in the cold in all common organic solvents and appreciably soluble in hot water. The *phenylurethane* separated from alcohol in needles, m. p. 197—198°, depressed by admixture with the isomeric phenylurethane (Found : N, 4·1%).

(2) The isomeride-α (0·2 g.) was heated with a solution of sodium (0·2 g.) in *iso*amyl alcohol (5 c.c.) for 2½ hours. The *iso*amyl alcohol was then removed in a current of steam, and the resultant oil collected by means of ether. The substance crystallised, and was recrystallised from aqueous ethyl alcohol. The product (0·1 g.) had m. p. 134—135° alone or when mixed with the isomeride-β.

2-*Keto*-1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 13 : 14 : 15 : 16-*dodecahydrochrysene* (V).—The above isomeride-α (1·6 g.) was dissolved in cold glacial acetic acid (18 c.c.), and a solution of chromic acid (0·48 g.; 1 atom O) in glacial acetic acid (15 c.c.) added drop-wise with cooling and stirring. The chromic acid was completely reduced after 12 hours and a mass of crystals had separated. The mixture was heated on the water-bath for 30 minutes and then diluted with water (15 c.c.). On cooling, the *ketone* separated (1·2 g.). It was recrystallised several times from glacial acetic acid and ethyl alcohol, separating in long needles, m. p. 145—146° (Found : C, 85·6, 85·7; H, 8·9, 8·7. $C_{18}H_{22}O$ requires C, 85·0; H, 8·7%). A further quantity of less pure material (0·3 g.) was obtained by dilution of the acetic acid mother-liquors. The ketone was moderately soluble in most solvents, freely in hot ethyl alcohol and acetic acid. The *oxime* separated from ethyl alcohol in long needles, m. p. 220—221° (decomp.) (Found : C, 80·7; H, 8·5; N, 5·2. $C_{18}H_{23}ON$ requires C, 80·3; H, 8·6; N, 5·2%). The semicarbazone was almost insoluble in all solvents, and sparingly soluble in hot ethyl alcohol, from which it separated in small prisms, m. p. 223—224°.

The most rigorous conditions, for example, boiling the sodio-derivative in dioxan with benzaldehyde, failed to give a benzylidene derivative, but the substance gave indications of the presence of a keto-methylene group in the test with β-resorcylaldehyde.

On oxidation under identical conditions, the isomeride-β yielded a product shown by m. p. and undepressed mixed m. p. to be the same as that obtained from the isomeride-α.

Attempted Methylation of 2-Ketododecahydrochrysene.—The sodio-derivative was formed from the ketone (2·0 g.) and sodamide (0·3 g.) by refluxing in dry benzene (50 c.c.) until no more ammonia was evolved (8 hours). Excess (2·0 g.) of methyl iodide was then added, and refluxing continued until the solution gave a neutral reaction to moist litmus (36 hours). Water was then added, and the benzene layer evaporated to dryness. The residue was taken up in hot ethyl alcohol (15 c.c.); the solution on cooling depositing unchanged substance (0·8 g.). The residue after removal of the solvent was distilled under diminished pressure, and the distillate converted in an oxime which, after one recrystallisation, had m. p. 216—218° alone or mixed with the oxime of the original saturated ketone. The mother-liquors both from the formation of the oxime and from the recrystallisation contained no appreciable amounts of any second substance.

Decahydrochrysene.—2-Ketodecahydrochrysene-A (3 g.) was gently refluxed with amalgamated zinc (10 g.), concentrated hydrochloric acid (20 c.c.), and a few drops of anisole for 18 hours. A further addition of hydrochloric acid (2 c.c.) was made every 3 hours. The yellow semi-solid product was taken up in ether, the ethereal solution dried and evaporated, and the residue distilled, yielding 0·5 g. of a pale yellow, viscous liquid, b. p. 170°/3 mm. The residue could not be distilled without decomposition and probably consisted of polymerisation products. The distillate was freely soluble in ether, light petroleum and benzene, sparingly soluble in cold ethyl alcohol. It crystallised from ether–alcohol on long standing in the ice-chest and was recrystallised from ethyl alcohol, forming long fine needles, m. p. 87—91° with sintering from 83°. As this behaviour was unaffected by further crystallisation, the substance was probably a mixture either of stereoisomerides or of the $\Delta^{1:13}$- and the $\Delta^{13:14}$-compound (Found : C, 90·5; H, 9·4. Calc. for $C_{18}H_{22}$: C, 90·8; H, 9·2%).

The crude semicarbazone of ketododecahydrochrysene (3 g.) was heated in a sealed tube with a solution of sodium (1·6 g.) in alcohol (20 c.c.) for 17 hours at 170°. The contents of the tube were then washed out with water, the flocculent white precipitate dissolved in ether, and the ethereal solution washed with water. On concentration of the ethereal solution to a small bulk the *product* crystallised (1 g.). It was purified by distillation (b. p. 170—180°/3 mm.), redistilled from sodium, and finally recrystallised from ethyl alcohol, separating in clusters of fine needles, m. p. 93—94° (Found: C, 90·8; H, 9·4. $C_{18}H_{24}$ requires C, 90·0; H, 10·0%. $C_{18}H_{22}$ requires C, 90·8; H, 9·2%).

Chrysene.—(a) Decahydrochrysene (0·6 g.) and selenium powder (3·5 g.) were heated together at 310—320° for 18 hours, the crystalline sublimate being repeatedly pushed back into the melt to ensure complete dehydrogenation. The final sublimate (0·4 g.) was resublimed at 250° from sodium, and the white sublimate (0·3 g.) recrystallised from benzene, forming characteristic plates, m. p. 248° alone or mixed with authentic chrysene (Found: C, 94·7; H, 5·3. Calc. for $C_{18}H_{12}$: C, 94·7; H, 5·3%). The *s.*-trinitrobenzene complex crystallised from benzene in yellow needles, m. p. 185°; Sudborough (J., 1916, **109**, 1344) gives m. p. 186°.

(b) Decahydrochrysene (0·08 g.) on similar treatment with selenium (0·4 g.) gave 0·02 g. of pure chrysene.

Dehydrogenation of Ketodecahydrochrysene-A.—The unsaturated ketone (1·0 g.) was heated with selenium (5 g.) for 18 hours at 320°. The crude sublimate (0·95 g.) was dissolved in hot ethyl alcohol (200 c.c.) and boiled with charcoal for 2 hours, and the filtrate concentrated to 80 c.c. Part of the material (0·2 g.) crystallised in rhomboidal plates and was identified as chrysene after recrystallisation from alcohol and benzene. The mother-liquor on concentration yielded a second substance (0·25 g.), much more soluble in ether and alcohol than chrysene. It was separated from chrysene by solution in ether and filtration from the undissolved chrysene and after recovery was repeatedly crystallised from glacial acetic acid, from which it separated in large hexagonal plates, stout needles, or rhomboidal plates, m. p. 210—220° (decomp.) after darkening at 205° (Found: C, 88·7; H, 4·9. $C_{18}H_{12}O$ requires C, 88·5; H, 4·9%).

The authors thank the University of New Zealand for a Travelling Scholarship awarded to one of them.

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