

856. *Syntheses of Perhydroanthracenes involving the Reduction of Thioketals with Lithium and Ethylamine. The Synthesis of 1,4,4a α ,5,8,8a β ,9,9a β ,10,10a α -Decahydroanthracene.*

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The unsaturated diketones (I) and (II) have been converted in good yields into the corresponding perhydroanthracenes by reduction of their bis(ethylene dithioketals) with lithium and ethylamine. A diene (XIII) required for the study of its addition reactions has been synthesised.

ALDER and STEIN¹ first condensed *p*-benzoquinone with butadiene (2 mol.) to give a product that they regarded as the diketone (I) or its stereoisomer with all-*cis*-bridgehead hydrogen atoms. We show below that this adduct has the structure (I), the second molecule of butadiene adding to the less hindered side of the bicyclic intermediate. The same conclusion has been reached by Hill and Martin² for this compound, and by de Vries, Heck, Piccolini and Winstein³ for the related adduct from *p*-benzoquinone and cyclopentadiene. Alder and Stein also isomerised the adduct (I) to the more stable diketone (II) under alkaline conditions, and they hydrogenated this diketone to the saturated diketone (III).

The primary objective in our work in this series was the synthesis of the diene (XIII), containing parallel double bonds and with the same stereochemistry as diketone (II). The synthesis of the diene is given below, but an approach involving the removal of carbonyl groups from the diketone (II) by the intermediate formation and reduction of a bisdithioketal was also attempted. The bis(ethylene dithioketal) (V) was formed from the diketone (II) and ethanedithiol in high yield by using boron trifluoride as catalyst. Desulphurisation of the thioketal by Raney nickel was slow,* and reduction was attempted by lithium and ethylamine.^{4,5} The reduction of the thioketal was not, however, appreciably faster than that of the olefinic bonds for, after complete removal of sulphur from the molecule, the known, saturated perhydroanthracene (VIII), m. p. 90°, was obtained. This structure is established by X-ray diffraction methods.⁶

The lithioethylamine technique is a new and effective way for reducing thioketals and the perhydro-compound (VIII) was also obtained by reduction of the thioketal (VI) from the saturated diketone (III). The procedure should not affect the stereochemistry of the bridgehead positions; preparation and reduction of the thioketal of the initial benzoquinone-butadiene adduct gave a perhydroanthracene, m. p. 121°. The following arguments indicate that this hydrocarbon has structure (VII), the original adduct therefore having structure (I). The hydrocarbon (VII) should exist in a relatively strainless three-chair-conformation. Nevertheless, as it contains two axial carbon substituents on the

* Hill and Martin² report the reduction of this thioketal to the saturated hydrocarbon in unstated yield by Raney nickel in boiling ethanol.

¹ Alder and Stein, *Annalen*, 1933, **501**, 247.

² Hill and Martin, *Proc. Chem. Soc.*, 1959, 390.

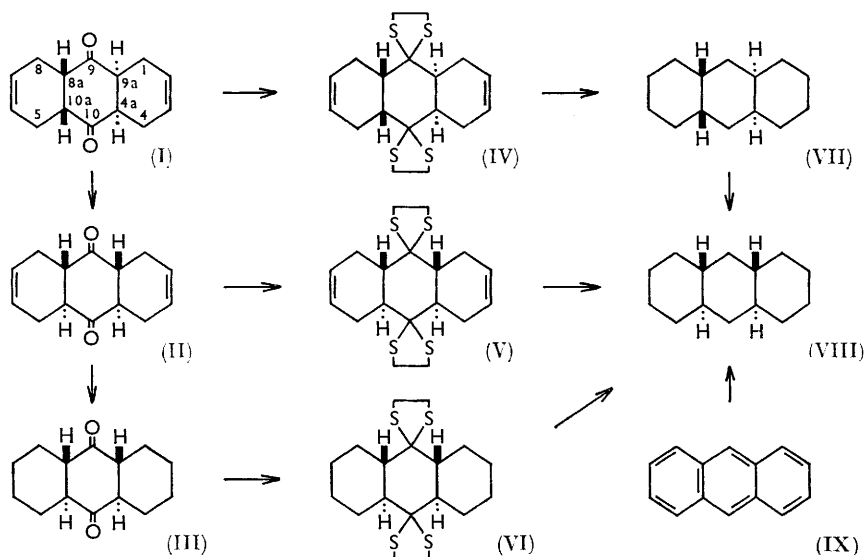
³ de Vries, Heck, Piccolini, and Winstein, *Chem. and Ind.*, 1959, 1416.

⁴ Benkeser and his co-workers, *J. Amer. Chem. Soc.*, 1955, **77**, 3230 and later papers.

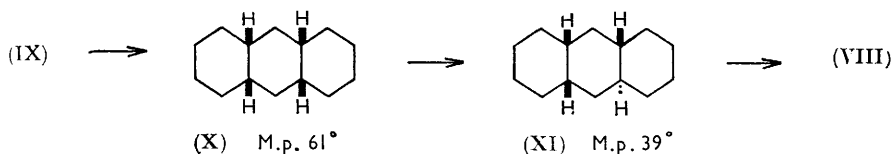
⁵ Hallsworth, Henbest, and Wrigley, *J.*, 1957, 1969; Hallsworth and Henbest, *J.*, 1957, 4604.

⁶ Bog, Hassel, and Vihorde, *Acta Chem. Scand.*, 1953, **17**, 1308.

central ring it will be of higher energy content than the isomer (VIII) containing only equatorial carbon substituents on the central ring⁷ (cf. isomerisation I \rightarrow II). The isomerisation (VII \rightarrow VIII) was effected by aluminium chloride in hexane. This most



stable perhydro-compound (VIII) was also obtained on reduction of anthracene (IX) with lithium and ethylenediamine; the mixture of perhydro- and dodecahydro-compounds reported by previous workers⁸ was ozonised, the unchanged saturated hydrocarbon then being easily isolated.



The preparation and interconversion of three (VIII, X, and XI) of the five possible perhydroanthracenes has been described by Cook, McGinnis, and Mitchell.⁹ Hydrogenation of anthracene gave the all-*cis*-compound (X), the steric course of hydrogenation being considered similar to that established in the phenanthrene series.¹⁰ This was isomerised by aluminium chloride to the lower-melting compound (XI) and then to the stable isomer (VIII). The stereochemical requirements of the Diels–Alder reaction mean that there must be *cis*-fusions of rings in the adduct from benzoquinone and butadiene, and in the perhydroanthracene of m. p. 121° derived by reduction of its bisdithioketal. The perhydro-compound must therefore have the structure (VII) or (X); by exclusion, the former structure is correct. This conclusion is in line with the results recently reported¹¹ for the hydrogenation of 2,6-dihydroxyanthracene. Clarke and Johnson showed that catalytic hydrogenation of this compound followed by oxidation gave two perhydro-2,6-diketones in about 8 : 1 ratio. The more abundant diketone was reduced to the hydrocarbon (X) and the less abundant diketone gave the hydrocarbon, m. p. 121° (*i.e.*, VII). (Comparison of the infrared absorption spectra of samples of the hydrocarbon prepared

⁷ Cf. Johnson, *J. Amer. Chem. Soc.*, 1953, **75**, 1498.

⁸ Reggel, Friedel and Wender, *J. Org. Chem.*, 1957, **22**, 891.

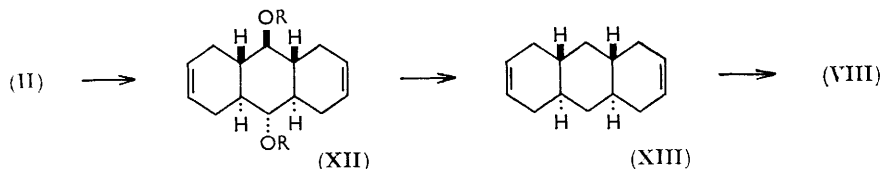
⁹ Cook, McGinnis, and Mitchell, *J.*, 1944, 286.

¹⁰ Linstead, Doering, Davis, Levine, and Whetstone, *J. Amer. Chem. Soc.*, 1942, **64**, 1985.

¹¹ Clarke and Johnson, *J. Amer. Chem. Soc.*, 1959, **81**, 5706.

by Dr. Clarke and by ourselves confirms that the same compound was obtained by the different routes.) The results are in accord with the known preference for *cis*-addition of hydrogen from a catalyst and the control of the direction of addition by steric factors.

Reduction of the saturated diketone (III) by the Wolff-Kishner method also gave the perhydroanthracene (VII), *trans* \rightarrow *cis* isomerisations occurring at the ring junctions. The formation, in Wolff-Kishner reductions, of deoxy-compounds related stereochemically to a less stable ketonic precursor has been noted before.¹² The evidence, in these cases, suggests that the less stable ketone (which is in equilibrium with the more stable form) reacts more quickly with hydrazine and hence the hydrocarbon related to it is formed.



In the present series, the diketone (III) partly isomerises to the full reduced derivative of diketone (I); this reacts rapidly with hydrazine with the consequent formation of the hydrocarbon (VII). Dr. R. L. Clarke (Sterling-Winthrop Institute, New York) has studied this reaction in greater detail, and by agreement, will report on it. Dr. Clarke has informed us that he and (independently) Dr. R. K. Hill and Mr. J. G. Martin of Princeton University, New Jersey, have also isolated the fifth perhydroanthracene from these reactions.

Preliminary results from a study of the structure of the hydrocarbon, m. p. 121°, by electron-diffraction methods also agree with structure (VII) (personal communication from Professor O. Hassel and K. Hjortaas, Oslo).

The 2,6-diene (XIII) was synthesised from the diketone (II). Reduction with sodium and butanol or, better, lithium and ammonia gave a dialcohol that can be assigned the diequatorial structure (XII; R = H). Its ditoluene-*p*-sulphonate was reduced in good yield by lithium aluminium hydride in tetrahydrofuran to the crystalline diene (XIII) and this was readily hydrogenated to the perhydro-compound (VIII). Addition reactions of the diene will be reported later.

EXPERIMENTAL

M. p.s were determined on a Kofler hot stage. Alumina (P. Spence, Grade H) was deactivated with dilute acetic acid. Light petroleum refers to the fraction of b. p. 60–80°. The $\alpha\beta$ -system of nomenclature¹³ is used for denoting relative configurations in racemic compounds. As none of these was resolved the (\pm)-prefix has been omitted throughout.

1,4,4 $\alpha\alpha$,5,8,8 $\alpha\beta$,9 $\alpha\alpha$,10 $\alpha\beta$ -Octahydroanthraquinone (I) and its Bis(ethylene Dithioketal) (IV).—*p*-Benzoquinone (210 g.), butadiene (280 g.), and benzene (400 c.c.) were heated in an autoclave at 100° for 24 hr. After cooling, the product was collected and washed with methanol to give the diketone (I) (250 g., 60%), m. p. 150–155°. The pure product had m. p. 154–155° (from benzene) (lit.,¹ m. p. 155°).

The diketone (I) (600 mg.) was dissolved in ethanedithiol (3 c.c.) at 20° and boron trifluoride-ether complex (0.5 c.c.) was added; almost immediately the product separated. After 30 min. it was filtered off and washed with methanol, giving the thioketal (IV) (960 mg., 94%), m. p. 254–255° (from dioxan-methanol) (Found: C, 58.9; H, 6.65; S, 34.2. C₁₈H₂₄S₄ requires C, 58.7; H, 6.55; S, 34.7%).

4 $\alpha\alpha$,8 $\alpha\beta$,9 $\alpha\beta$,10 $\alpha\alpha$ -Perhydroanthracene (VII).—The bisdithioketal (IV) (1.1 g.) was suspended in ethylamine (100 c.c.). Small pieces of lithium (870 mg.) were added; the flask was then stoppered, cooled to –20°, and shaken for 45 min. with periodic release of the pressure. Water was then added to discharge the blue colour and the ethylamine was allowed to evaporate

¹² Djerassi, Grossnickle and High, *J. Amer. Chem. Soc.*, 1956, **78**, 3166; also unpublished results of Professor W. S. Johnson (Stanford) and his co-workers.

¹³ Henbest, Smith, and Thomas, *J.*, 1958, 3293.

overnight. The product was extracted with light petroleum (b. p. 40—60°), and the extracts were filtered through alumina (10 g.) to give the perhydroanthracene (VII) (480 mg., 86%), m. p. 120—121° (from acetone) (Found: C, 87.5; H, 12.5. Calc. for C₁₄H₂₄: C, 87.4; H, 12.6%)

1,4,4a α ,5,8,8a β ,9a β ,10a α -Octahydroanthraquinone (II) and Reduction of its Bisdithioketal (V).—The diketone (I) (50 g.) in dioxan (400 c.c.) and methanol (100 c.c.) was heated almost to the b. p. under nitrogen, and 10% potassium hydroxide in methanol (5 c.c.) was added. On cooling, the diketone (II) (45 g., 90%) separated, having m. p. 244—245° (from ethyl acetate) (lit.,¹ m. p. 244°).

The diketone (II) 1.85 g.) was dissolved in ethanedithiol (3 c.c.), and boron trifluoride-ether complex (2.5 c.c.) was added. After 6 hr. at 20° the product was filtered off and washed with methanol to give the bis(ethylene dithioketal) (2.6 g., 82%), m. p. 284—285° (from dioxan-methanol) (Found: C, 58.3; H, 6.4%).

By the above procedure the bistioketal (770 mg.) was reduced with lithium in ethylamine to the perhydroanthracene (VIII) (350 mg., 90%), m. p. and mixed m. p. 89—90° (from methanol) (lit.,⁹ m. p. 89—90°). The same perhydro-compound was obtained by using a reaction time of 30 min. or more. When reduction was stopped shortly after the appearance of the blue colour a mixture of hydrocarbons was isolated.

4a α ,8a β ,9a β ,10a α -Dodecahydroanthraquinone (III) and Reduction of its Bisdithioketal (VI).—The diketone (II) (2.7 g.) was hydrogenated in ethyl acetate (250 c.c.) with 2% palladium-calcium carbonate (uptake 560 c.c. at 20°/1 atm.; theor., 550 c.c.). Removal of catalyst and solvent gave the saturated diketone (III), m. p. 245—246° (from ethyl acetate) (lit.,¹ m. p. 244°).

The diketone (III) (1 g.) with ethanedithiol (3 c.c.) and boron trifluoride-ether complex (2.5 c.c.), as above, gave the saturated bis(ethylene dithioketal) (VI) (1.6 g., 94%), m. p. 263—264° (from dioxan-methanol) (Found: C, 58.35; H, 7.6; S, 34.6. C₁₈H₂₈S₄ requires C, 58.05; H, 7.6; S, 34.35%). On reduction with lithium-ethylamine as above, this thioketal (620 mg.) gave the perhydro-compound (VIII) (340 mg.).

4a α ,8a β ,9a β ,10a α -Perhydroanthracene (VIII).—(a) From the perhydroanthracene (VII). A mixture of the hydrocarbon (VII) (500 mg.), powdered anhydrous aluminium chloride (800 mg.) and hexane (3 c.c.) was kept at 20° with occasional shaking for 5 days. The product was isolated with hexane, the extracts being filtered through alumina to give the perhydro-compound (VIII) (220 mg.), m. p. and mixed m. p. 89—90° (from methanol).

(b) From anthracene. Anthracene (4 g.) in ethylenediamine (250 c.c.) was stirred under nitrogen at 100° \pm 5°. Small pieces of lithium (13 g.) were added during 2.5 hr. and heating was maintained for a further 3 hr. The mixture was poured into ice and water, and the product isolated with ether. The resulting brown oil was decolorised by filtering its solution in light petroleum (b. p. 40—60°) through alumina (50 g.). The product (3.5 g.), in ethyl acetate (50 c.c.), was cooled to -30° and treated with ozonised oxygen at the rate of 10 l./hr. for 3.5 hr. 2% Palladium-calcium carbonate was then added and the mixture was shaken with hydrogen, 127 c.c. being absorbed (at 20°/1 atm.). Removal of catalyst and solvent gave a yellow gum that was extracted with light petroleum (b. p. 40—60°). Filtration of the extracts through alumina (20 g.) gave the perhydroanthracene (320 mg., 7%), m. p. and mixed m. p. 89—90° (from methanol).

1,4,4a α ,5,8,8a β ,9,9a β ,10a α -Decahydroanthracene-9 β ,10 α -diol (XII; R = H) and its Di-toluene-p-sulphonate.—(a) The diketone (II) (10 g.) in tetrahydrofuran (500 c.c.) was added dropwise with stirring to lithium (5 g.) in liquid ammonia (1 l.), the mixture being further stirred for 3 hr. The excess of lithium was decomposed with methanol, and the ammonia was evaporated. The residue was cooled in ice and acidified with 6N-hydrochloric acid. The product (7 g., 72%) was filtered off and washed with acetone (m. p. 270—272°). The pure diol had m. p. 274—275° (from ethanol) (Found: C, 75.9; H, 8.9. C₁₄H₂₀O₂ requires C, 76.3; H, 9.15%).

(b) The diketone (II) (2 g.) was treated with an excess of sodium (8 g.) in stirred boiling butan-1-ol (200 c.c.) under nitrogen. The mixture was heated under reflux for 1 hr., cooled, and diluted with ethyl acetate and water. The organic layer was separated, then evaporated, and the residue, after being washed with benzene, crystallised from ethanol to give the diol (250 mg., 25%), m. p. and mixed m. p. 274—275°.

The diol (5 g.) and toluene-*p*-sulphonyl chloride (20 g.) in pyridine (100 c.c.) were kept at 40° for 3 days. Part of the product separated and this was removed by filtration; water was

added to the mother-liquor to precipitate the rest of it. Crystallisation from dioxan gave the *ditoluene-p-sulphonate* (9.2 g., 77%), m. p. 201—202° (Found: C, 63.6; H, 5.9. $C_{28}H_{32}O_6S_2$ requires C, 63.6; H, 6.1%).

1,4,4 α ,5,8,8 $\alpha\beta$,9,9 $\alpha\beta$,10,10 $\alpha\alpha$ -*Decahydroanthracene* (XIII).—The preceding diester (8.6 g.) was placed in a Soxhlet extractor over lithium aluminium hydride (10 g.) in boiling tetrahydrofuran (400 c.c.), being extracted during 2 days. The mixture was heated under reflux for a further 8 days. Excess of hydride was then decomposed with water and, after filtration, the solvent was evaporated. The residue was extracted with light petroleum (b. p. 40—60°), and the extracts were passed through alumina (50 g.). Removal of solvent under reduced pressure gave the *diene* (XIII) (2.4 g., 78%), m. p. 112—113° (from acetone) (Found: C, 89.2; H, 10.45. $C_{14}H_{20}$ requires C, 89.3; H, 10.7%).

The diene reacted with the theoretical amounts of bromine and hydrogen; in the latter case the perhydroanthracene (VIII), m. p. and mixed m. p. 88—89°, was obtained in good yield.

The authors thank Drs. J. W. Cook and J. D. Loudon for samples of perhydroanthracenes, and the University of London and the Department of Scientific and Industrial Research for research grants (to N. S. C.). They also acknowledge very helpful correspondence with Dr. R. L. Clarke and Professors O. Hassel and W. S. Johnson.

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[Received, February 29th, 1960.]
