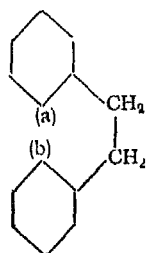


ON A NEW METHOD OF SYNTHESIS OF PHENANTHRENE DERIVATIVES

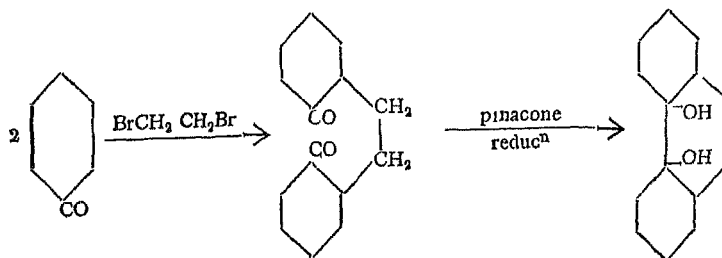
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Owing to its existence in a large number of important natural products such as sterols, bile acids, sex hormones and plant heart poisons, the phenanthrene ring has won for itself a place of unique interest and importance in synthetic chemistry. Besides the classical synthesis of phenanthrene by Pschorr (*Ber*, 29, 496), a number of new methods have been developed for the synthesis of this hydrocarbon, notable and more important among these being the syntheses by Haworth (*J C S*, 1932, 1125, 2248, 2717, 2720) and by Bardhan and Sengupta (*J C S*, 1932, 2520, 2798). It is natural that methods involving a number of steps and employing drastic reactions could not be employed with ease and success for preparing derivatives of phenanthrene which might be required as starting substances for the synthesis of substances occurring in nature, and their degradation products. The present work was undertaken with a view to evolving a facile method for the synthesis of phenanthrene derivatives which could be conveniently used as starting materials for further operations leading ultimately to the synthesis of natural products.

The synthetic route we tried to develop consisted, essentially, in preparing a suitable derivative of dicyclohexyl ethane such as

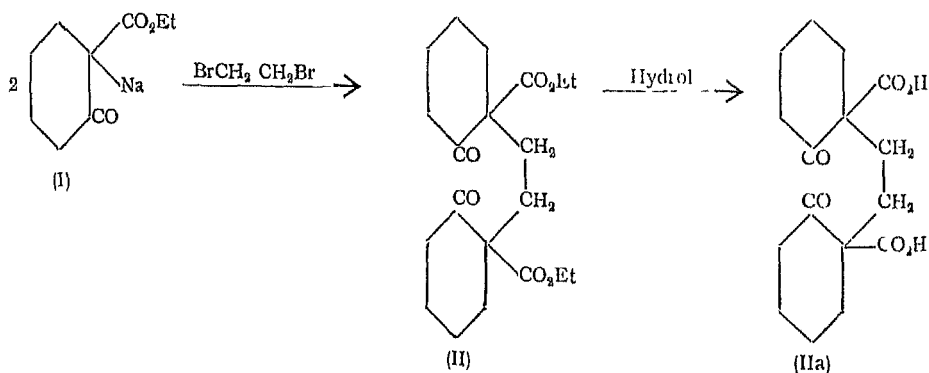


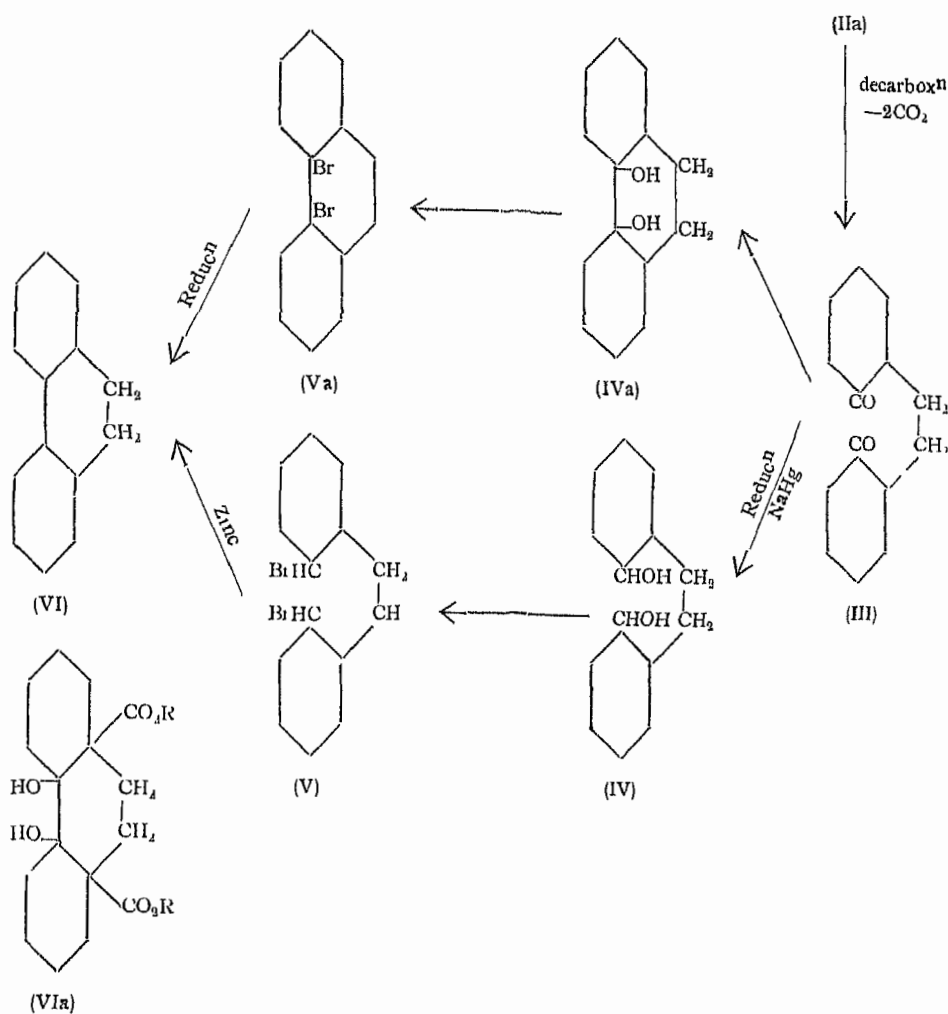
and then bridging up the carbon atoms marked (a) and (b) and the following scheme of synthesis was attempted first



It is known by the work of Halle¹ (*Compt rend*, **157**, 179) that *cyclohexanone* could be directly alkylated with alkyl iodide in the presence of sodamide. Following his method, a solution of *cyclohexanone* in absolute ether was treated with molecular proportion of sodamide. Then half a molecular proportion of ethylene bromide was added and the whole thing gently refluxed. In this case, no reaction took place. With a view to finding out whether a higher temperature might induce the reaction to take place, the experiment was repeated by using toluene in place of ether and by heating at elevated temperature in an autoclave. Even under such drastic conditions the reaction did not proceed in the desired direction, much of the *cyclohexanone* remaining unreacted. A small quantity of a compound, b.p. 136–38°/10 mm. was obtained and proved to be *cyclohexylidene-cyclohexanone*, formed presumably by the self-condensation of *cyclohexanone* in the presence of sodamide.

Having found that *cyclohexanone* could not be used as a starting material for our work, we next tried the action of ethylene bromide upon the sodium derivative of ethyl *cyclohexanone-2-carboxylate* with the hope that the resulting condensation product (II) could ultimately be converted (via IV, V or IVa, Va) to a phenanthrene compound (VI) according to the scheme outlined below.





The sodium derivative of ethyl *cyclohexanone-2-carboxylate* (I) was condensed with half a molecular proportion of ethylene bromide in alcoholic solution when a 40 per cent yield of the diketo ester (II), b p 127-29°/20 mm, was obtained. With hydrazine hydrate it gave a pyrazalone derivative, m p 295°. The yield of the diketo ester was improved to 60 per cent by using the potassium derivative of ethyl *cyclohexanone-carboxylate* in xylene suspension.

With a view to effecting simultaneous hydrolysis and decarboxylation, the diketo ester (II) was heated with hydrochloric acid (19%).

It was found that this treatment with hydrochloric acid, resulted only in the hydrolysis of the ester to the corresponding dicarboxylic acid (IIa). Increasing the duration of heating with hydrochloric acid did not bring about the decarboxylation. The dicarboxylic acid did not lose carbon dioxide even at its melting point. The same dicarboxylic acid (IIa) was obtained by prolonged hydrolysis of the diketone ester (II) with alkali. The remarkable stability of this acid can only be explained by the fact that the carboxyl groups are situated in tertiary positions.

Since it was not feasible to convert the diketone ester (II) into the corresponding diketone (III) the reduction of the ester itself to (VIa) was next tried. Following the method of Barnet and Lawrence (*JCS*, 1935, 1105) who prepared 1,1'-dihydroxy dicyclohexyl by subjecting cyclohexanone to pinacone reduction, it was expected that by submitting the diketone-ester to a similar pinacone reduction, a dihydroxy derivative of phenanthrene (VIa) might be straightaway obtained. In one experiment, the pinacone reduction was carried out with aluminium amalgam and in another with magnesium amalgam. The reduction did not proceed at all in any of these two experiments.

Finding that the pinacone reduction of the diketone-ester (II) was unsuccessful, we thought of reducing the two keto-groups in (II) to secondary alcoholic groups. To effect this, we treated the diketone-ester (II) with 3.5 per cent sodium amalgam. Surprisingly enough, no reduction took place.

EXPERIMENTAL

Attempts to Condense cyclohexanone with Ethylene Bromide

To cyclohexanone (98 g.) dissolved in absolute ether (400 c.c.) was added sodamide (39 g.) in the form of powder, little by little. Then ethylene bromide (94 g.) was added to the mixture, apparently without any reaction taking place. The mixture was then gently refluxed for 6 hours. The product was then poured in water and the ethereal layer separated and dried with anhydrous magnesium

sulphate The ether was distilled and the residue on distillation gave only *cyclohexanone*

In another experiment, to a solution of *cyclohexanone* (19.6 g) in dry toluene (50 c c) was added sodamide (7.8 g) The mixture after the addition of ethylene bromide (18.8 g) was heated in an autoclave at 140° for 9 hours The reaction product was worked up as above After distilling the toluene, the residue was found to yield 13.5 g of *cyclohexanone* and 2.5 g of an oil boiling at 136–38°/10 mm This oil was identified as *cyclohexylidene-cyclohexanone* by preparing the oxime, m p 146–48°

Condensation of Ethyl Cyclohexanone-2-Carboxylate with Ethylene Bromide Formation of the Diketo-Diester (II)

In an one litre round-bottomed flask fitted with a reflux condenser carrying a calcium chloride tube was placed 400 c c of absolute alcohol and sodium (23 g), cut into small pieces was slowly added to it After the addition of sodium was complete, freshly distilled ethyl *cyclohexanone-2-carboxylate* (170 g) was gradually added The formation of the sodium derivative took place almost immediately The addition of ethylene bromide (94 g) was then made, little by little, under cooling After the addition of the ethylene bromide was complete, the reaction mixture was allowed to remain at room temperature for 1 hour and was then heated under reflux on a water-bath for 6 hours The mixture was then poured into a large volume of water and the oily layer thus formed was separated The aqueous layer was extracted twice with ether, and the ethereal extract was added to the oily portion The combined ethereal extract was dried over anhydrous magnesium sulphate, ether distilled and the residual oil was distilled under reduced pressure The main fraction, which was found to consist of the diketo-ester (II), came off at 127–29°/10 mm as a transparent colourless oil having a characteristic smell highly reminiscent of cow's ghee, yield 40 per cent A pure sample of the ester, obtained by redistillation gave the following results on analysis (Found C, 65.46, H, 8.27 $C_{20}H_{30}O_6$ requires C, 65.57, H, 8.20 per cent)

*Condensation of Ethyl Cyclohexanone-2-Carboxylate with
Ethylene in Xylene*

Molecular potassium (13 g) was placed under dry xylene (300 c c) contained in a round-bottomed flask fitted with a reflux condenser carrying a calcium chloride guard tube. Ethyl cyclohexanone-2-carboxylate (5.7 g) was added gradually when the formation of the potassium derivative took place fairly vigorously. After the addition of the ester was over, ethylene bromide (31 g) was added, drop by drop under cooling and the mixture was heated under reflux for 10 hours. It was then poured in water and the diketo diester (II) was isolated as in the previous experiment, the yield being 60 per cent in the present instance. A small amount of a viscous oil came over at 175–81°/10 mm, which was not further investigated.

Pyrazalone Derivative of the Diketo-Ester

The diketo-ester (3.6 g) was dissolved in alcohol (20 c c) and hydrazine hydrate (1 g) was added to it, and the mixture heated on a water-bath for about 5 minutes, when the pyrazalone derivative separated as a crystalline solid. The solid was filtered under suction and was washed with water. It was recrystallised from a large amount of alcohol in the form of colourless shining plates, m.p. 296°.

*Attempted Decarboxylation of the Diketo-Ester with Hydrochloric
Acid Formation of the Diketo Acid*

Hydrochloric acid (19%, 100 c c) was added to the diketo ester (12.5 g), and the mixture was heated under reflux for 12 hours. It was found that no carbon dioxide was evolved during the course of the reaction. At the end of 12 hours, the ester had gone completely into solution. The solution was then evaporated on a water-bath almost to dryness, when a solid began to separate. The solid was collected and after treatment with animal charcoal, was crystallised from a mixture of acetone and water in the form of colourless long, slender needles, m.p. 102–3°. It was proved to be an acid, which did not lose

carbondioxide even at 220° The melting point of the acid remained constant on further crystallisation (Found C, 61.81, H, 7.16, Equiv Wt, 152.9. $C_{16}H_{22}O_6$ requires C, 61.93, H, 7.08 per cent, Equiv Wt, 155)

*Treatment of the Ester (II) with Alkali Formation
of the Acid (IIa)*

The ester (5 g) was hydrolysed by heating with 8 per cent KOH for 18 hours. The acid was isolated in the usual manner, m.p. 102–3°, and was found to be identical with the acid obtained above.

Pinacone Reduction of Diketo-Ester (II)

The diketo-ester (18.3 g) was dissolved in dry benzene (40 c.c.) contained in a flask with a reflux condenser. Coarse aluminium powder (1.75 g) was then added, followed by mercuric chloride (0.7 g). The mixture was heated for 1 hour on a water-bath with frequent shaking. Then water (20 c.c.) was added, gradually, followed up by benzene (50 c.c.). The mixture was heated for a further period of 1 hour and the hot mixture filtered, the solid was extracted with 50 c.c. of boiling benzene. The united filtrates were concentrated on a water-bath, cooled, light petrol added and the whole thing thoroughly cooled. No solid separated on cooling. The petrol was then removed by distillation, and the residual oil was distilled. The oil came over at 127–29°/10 mm, and was found to consist entirely of the unchanged diketo-ester (II).

The experiment was repeated using magnesium powder in place of aluminium powder with no better result, the diketo-ester being recovered unchanged.

Reduction of the Diketo Ester (II) with Sodium Amalgam

Into a 250 c.c. 3-necked flask fitted with an efficient stirrer was placed a mixture of 100 c.c. alcohol and water. The diketo-ester (10 g) was then added. The stirrer was then started and a vigorous stream of carbon-dioxide was passed through the mixture.

throughout the duration of the experiment. Sodium amalgam (3.5%, 200 g) was then added gradually. The addition of the amalgam was done very gradually, in small lots at a time, each instalment being added after the preceding ones had completely reacted. The addition of the entire amount of the amalgam occupied about 8 hours. After the addition of the amalgam was over, the stirring was continued for a further period of half-an-hour.

The reaction mixture was then transferred to a separating funnel. The mercury remaining at the bottom was separated and was washed with ether. The water-alcohol layer, containing the product of the reaction, was thoroughly extracted with ether. The ethereal extract was washed with water and was dried over anhydrous magnesium sulphate. The ether was distilled from the dry ethereal extract and the residual oil distilled under reduced pressure. Almost all the oil came over at 127–29°/10 mm, leaving behind only one or two drops of an oil in the distilling flask. The boiling point and the smell of the distillate pointed out to the probability of its being the unchanged diketo-ester. The fact that the distillate was really the unchanged ester was proved by preparing the pyrazalone derivative, m.p. 296°.

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