[Contribution from the Department of Chemistry, Panjab University, and the Department of Organic Chemistry, Indian Association for the Cultivation of Science]

FRIEDEL-CRAFTS REACTION INVOLVING UNSATURATED KETONES AND ESTERS. III. A NEW ROUTE TO BENZO[c]PHENANTHRENE DERIVATIVES

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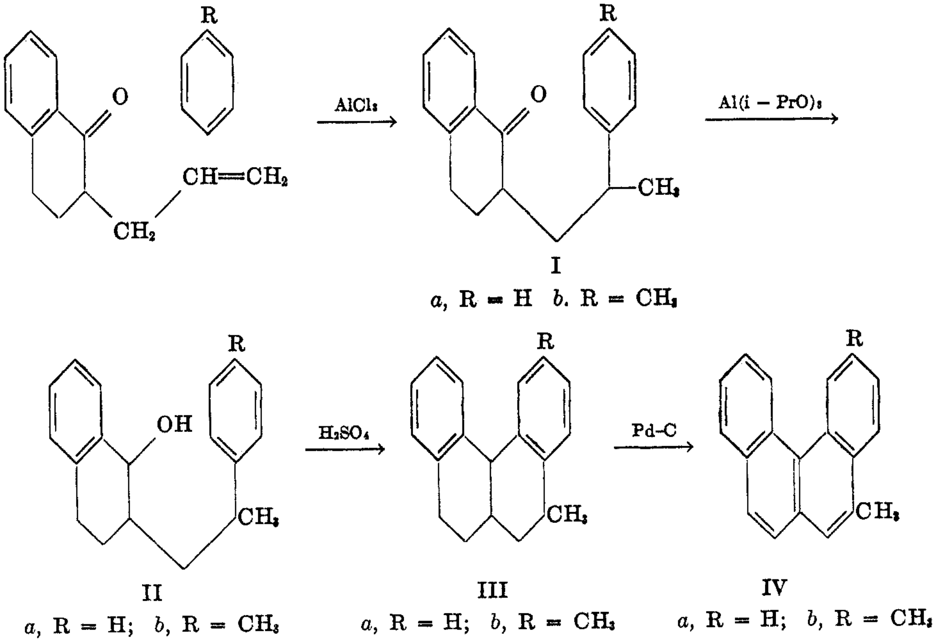
Since the discovery of the carcinogenic activity of benzo[c]phenanthrene (1), considerable interest has been displayed in this group of polycyclic aromatic hydrocarbons. This interest was further accentuated by the observation (2) that 5-methylbenzo[c]phenanthrene is a very potent carcinogen. As a sequel to this, a number of methods for the synthesis of benzo[c]phenanthrene and its derivatives have been developed (3). Most of these methods are, however, laborious and involve numerous steps resulting in low over-all yield, although Wilds and Werth (4) have recently reported an elegant synthetic route to these compounds. The present communication describes a new and convenient method of synthesis of 5-methylbenzo[c]phenanthrene and 2,5-dimethylbenzo[c]phenanthrene, which promises general applicability to the synthesis of a variety of benzo[c]phenanthrene derivatives.

FORMULAE



I
a, R = H b. R = CH₃

II
a, R = H; b, R = CH₃

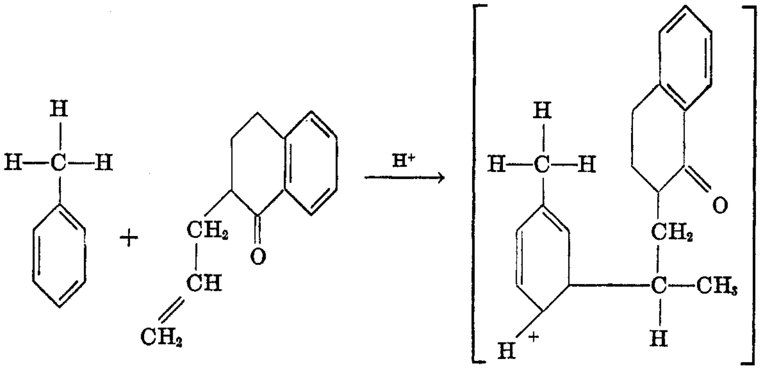
III
a, R = H; b, R = CH₃

IV
a, R = H; b, R = CH₃

The present method has been developed on the model of the synthesis of 9-methylphenanthrene by Mukherji and Bhattacharyya (5), the starting material being 2-allyl-1-tetralone, which was prepared by allylation of 2-hydroxymethylene-1-tetralone and subsequent hydrolysis of 2-allyl-2-formyl-1-tetralone following the method of Kloetzel (6). A Friedel-Crafts reaction of 2-allyl-1-tetralone with benzene was accomplished satisfactorily according to the conditions of Mukherji and Bhattacharyya (5) to give Ia in 82% yield. Reduction of Ia by the Ponndorf method proceeded smoothly to yield almost quantitatively the corresponding carbinol (IIa) which was cyclized by conc'd sulfuric acid (7) to IIIa in 70% yield. Dehydrogenation of IIIa with palladium-charcoal (30%) (8) gave 5-methylbenzo[*c*]phenanthrene (IVa) (3) in excellent yield.

Similarly, 2-allyl-1-tetralone was treated with toluene in the presence of aluminum chloride to give Ib. Proof of the *para*-orientation in Ib was obtained by its alkaline permanganate oxidation to a mixture of phthalic and terephthalic acids which were easily separated by fractional crystallization from water. Terephthalic acid was identified through its dimethyl ester. No trace of isophthalic acid was found in the oxidation product. This result is rather intriguing in view of the recent finding in this laboratory that toluene condenses with ethyl allylacetate under comparable conditions to give the *meta*-orientated product (11). The postulation (13) of the formation of an intermediate trialkylated product followed by dealkylation hardly explains the formation of *meta*-orientated products from toluene and alkyl halides having large alkyl groups. Condon (14) showed that *meta* alkylation proceeds by a direct rather than by an isomerization or an alkylation-dealkylation process. Hennion, Driesch, and Dee (15) have recently demonstrated that the preponderance of the *para* isomer in the *tert*-butylation of isopropylbenzene and that of the *meta* isomer in the isopropylation of *tert*-butylbenzene could be explained only on the basis of the steric factor involved.

It is evident that the alkyl group introduced as in the case of Ib is much larger than the group introduced in the reaction between toluene and ethyl allylacetate. As a result, the steric interference between the alkylating group and the existing methyl group will be much greater in case of *meta* condensation between toluene and 2-allyl-1-tetralone.



Thus *para* condensation in the case of Ib in contrast with the *meta* orientation in the reaction between toluene and ethyl allylacetate (11) can be reasonably explained on the basis of the steric interference involved in such processes (15).

The ketone (Ib) was subjected to the same sequence of reactions as Ia when the hitherto unknown 2,5-dimethylbenzo[*c*]phenanthrene was obtained in satisfactory over-all yield.

This method is now being extended to syntheses of a variety of methoxy derivatives of benzo[*c*]phenanthrene, which will form the starting materials for another series of investigations.

EXPERIMENTAL

The melting points and boiling points are uncorrected.

The analyses marked (*) were by Drs. Weiler and Strauss, Oxford.

2-Hydroxymethylene-1-tetralone. This was previously prepared by others (9) in good yield, and a similar procedure (10) was adopted for the present preparation.

2-Allyl-1-tetralone. To an ice-cold suspension of dry sodium ethoxide (prepared from 3.8 g. of sodium) in dry benzene (150 ml.), 26.1 g. of 2-hydroxymethylene-1-tetralone was slowly added with stirring when the sodium salt separated gradually. After standing overnight allyl iodide (33.6 g.) was added in the cold and the mixture was refluxed on the steam-bath until the supernatant layer failed to respond to a ferric chloride test (about 6 hours). The reaction mixture then was decomposed with acidulated water, and the benzene layer was washed and dried. After the removal of the solvent the residue on distillation in a vacuum gave 24 g. of 2-allyl-2-formyl-1-tetralone as an oil, b.p. 134–138°/1 mm. The ferric chloride test was negative even after standing for 24 hours.

The above oil was hydrolyzed by stirring with 160 ml. of 5% sodium hydroxide solution at 50–55° for three hours, followed by acidification and steam-distillation of the mixture. The oil in the distillate was taken up in ether and after the usual working up and removal of the solvent, the residue on distillation gave 26.5 g. (82%) of 2-allyl-1-tetralone, b.p. 144–150°/5 mm., n_D^{30} 1.5511, as a colorless oil with a camphoraceous smell.

Anal. Calc'd for $C_{13}H_{14}O$: C, 83.87; H, 7.53.
Found: C, 83.56; H, 7.28.

The *semicarbazone* was prepared by refluxing 1 g. of II, 1.7 g. of semicarbazide hydrochloride, and 1.5 ml. of pyridine in 15 ml. of methyl alcohol on a steam-bath for 4 hours. After three crystallizations from ethanol the m.p. 183–184° did not change. Previously reported (12), m.p. 174–175° was obtained after one crystallization only.

Anal. Calc'd for $C_{14}H_{17}N_3O$: N, 17.28. Found: N, 16.60.

2-(β-Methyl-β-phenylethyl)-1-tetralone (Ia). In a three-necked flask (500 ml.) provided with a mercury-sealed stirrer, a guard tube, and a thermometer was placed 150 ml. of thiophene-free dry benzene and 9.3 g. of 2-allyl-1-tetralone, the temperature being maintained below 10°. A total of 15 g. of finely powdered anhydrous aluminum chloride was added with stirring in three portions (8 g., 4 g., and 3 g.) over a period of one hour. After the addition was complete, the stirring was continued for another three hours and during the later stage of this period the temperature was allowed to rise to 20°. The reaction mixture was then decomposed with ice-cold hydrochloric acid and the benzene layer, after being worked up in the usual way, gave on distillation in a vacuum an 82% yield of Ia, b.p. 185–192°/1 mm. (mainly at 190°/1 mm.) as a viscous oil, n_D^{30} 1.5759.

Anal. Calc'd for $C_{19}H_{20}O$: C, 86.36; H, 7.57.
Found: C, 86.12; H, 7.62.

This compound failed to give any *semicarbazone* by the usual method.

2-(β-Methyl-β-phenylethyl)-1-tetralol (IIa). The above ketone (Ia, 5.5 g.) was reduced to the corresponding carbinol with aluminum isopropoxide prepared from 2.5 g. of aluminum and 75 ml. of isopropyl alcohol. The reaction mixture after being worked up in the usual way was distilled to give an 86% yield of IIa, b.p. 210–215°/4 mm., $n_D^{31.5}$ 1.5908.

Anal. Calc'd for $C_{19}H_{22}O$: C, 85.71; H, 8.27.
Found: C, 85.2; H, 8.36.

5-Methyl-5,6,6a,6b,7,8-hexahydrobenzo[*c*]*phenanthrene* (IIIa). The carbinol (IIa; 2 g.)

was cooled in an ice-bath, 1.7 ml. of concentrated sulfuric acid (*sp. gr.* 1.84) was added, and the contents were mixed intimately. After three hours the reaction mixture was diluted with water and worked up with ether in the usual way. The product was distilled under 2 mm. pressure from a bath at 195° when it was obtained as a gummy substance, n_D^{31} 1.5994; yield, 1.3 g. (70%).

Anal. Calc'd for $C_{19}H_{20}$: C, 91.93; H, 8.06.
Found: C, 91.87; H, 7.96.

5-Methylbenzo[c]phenanthrene (IVa). The hexahydro compound (IIIa, 1 g.) was smoothly dehydrogenated by heating with 0,1 g. of palladium-charcoal (30%) for four hours at 300–320°. 5-Methylbenzo[*c*]phenanthrene, obtained as a very viscous oil on sublimation in a vacuum, was crystallized from acetone-alcohol in light yellow needles, m.p. 70–71°. On further crystallization from alcohol with Norit, fine colorless needles, m.p. 71–72° [reported (3a) m.p. 69.5–70°; (3b) m.p. 70.4–71°] was obtained. The total yield of the crystallized product was 0.6 g.

Anal. Calc'd for $C_{19}H_{14}$: C, 94.21; H, 5.78.
Found: C, 94.07; H, 5.90.

The *picrate* was obtained from ethanol in vermillion needles, m.p. 135–136° [reported (3b) m.p. 141.8–143.2°].

*Anal.** Calc'd for $C_{25}H_{17}N_3O_7$: C, 63.69; H, 3.60; N, 8.91.
Found: C, 63.13; H, 3.51; N, 8.75.

2-[β-Methyl-β-(p-tolyl)ethyl]-1-tetralone (Ib). 2-Allyl-1-tetralone (9.0 g.) was treated with pure toluene (150 ml.) in the presence of aluminum chloride under the same conditions as in the case of Ia, when 8.6 g. (64%) of (Ib) was obtained, b.p. 240°/13–14 mm., n_D^{25} 1.5718.

Anal. Calc'd for $C_{20}H_{22}O$: C, 86.33; H, 7.91.
Found: C, 86.26; H, 8.14.

The *2,4-dinitrophenylhydrazone* (0.7 g. from 0.5 g. of Ib) was prepared in the usual manner (crude m.p. 178–182°) and was crystallized as deep orange needles from ethyl acetate, m.p. 192–193°.

*Anal.** Calc'd for $C_{26}H_{26}N_4O_4$: N, 12.22. Found: N, 12.20.

One gram of the ketone (Ib) was oxidized with alkaline potassium permanganate according to the standard conditions (16) when 0.8 g. of a mixture of phthalic and terephthalic acids was obtained. The latter (0.3 g.) was separated by taking advantage of its insolubility in hot water, and was converted into its dimethyl ester, m.p. 140°, undepressed when mixed with an authentic sample of dimethyl terephthalate.

2-[β-Methyl-β-(p-tolyl)-ethyl]-1-tetralol (IIb). The above ketone (Ib; 5 g.) was reduced with aluminum isopropoxide (prepared from 2.5 g. aluminum in 75 ml. of isopropyl alcohol) in the usual way when the carbinol (IIb) was obtained as a colorless viscous oil, b.p. 180–182°/1 mm., n_D^{25} 1.5789; yield, 4.1 g. (81%).

Anal. Calc'd for $C_{20}H_{24}O$: C, 85.71; H, 8.57.
Found: C, 85.38; H, 8.23.

2,5-Dimethyl-5,6,6a,6b,7,8-hexahydrobenzo[c]phenanthrene (IIIb).

Cyclization of the carbinol (IIb; 2 g.) was effected with 2 ml. of H_2SO_4 (*sp. gr.* 1.84) in the same manner as described earlier and the cyclized product (IIIb) obtained boiled at 180–185°/3–4 mm., n_D^{27} 1.5884; yield, 1.2 g. (66%).

Anal. Calc'd for $C_{20}H_{22}$: C, 91.60; H, 8.40.
Found: C, 91.27; H, 8.36.

2,5-Dimethylbenzo[c]phenanthrene (IVb). The hexahydro compound (IIIb; 2 g.) was heated with 0.2 g. of 30% palladium-charcoal at 300–320° for 4 hours. From the reaction mixture 1.4 g. (61.5%) of 2,5-dimethylbenzo[*c*]phenanthrene was obtained as a pale yellow viscous oil, 190–195°/2 mm., which solidified after regeneration from its *picrate* (vide infra) and was crystallized from ethyl alchol, m.p. 91–92°.

Anal. Calc'd for $C_{20}H_{16}$: C, 93.75; H, 6.25.
Found: C, 93.61; H, 6.32.

The *picrate* was prepared from 1.0 g. of IVb in the usual manner and was twice crystallized as deep orange needles from ethanol, m.p. 146–147°; yield, 1.4 g.

*Anal.** Calc'd for $C_{20}H_{16} \cdot C_6H_3N_3O_7$: N, 8.66. Found: N, 8.30.

SUMMARY

A new method for the synthesis of benzo[*c*]phenanthrene derivatives has been developed and the syntheses of 5-methyl- and 2,5-dimethyl-benzo[*c*]-phenanthrene have been described.

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