[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

The Dienone–Phenol Rearrangement in the Benzo(c)phenanthrene Series. A Case of Concurrent Methyl and Methylene Migration

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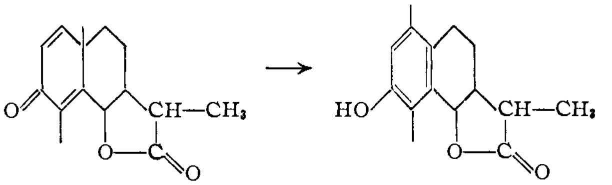
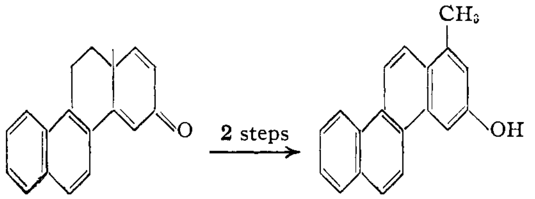
The synthesis of 2-keto-4a-methyl-2,4a,5,6-tetrahydrobenzo(c)phenanthrene (XVIII) is described. Dienone–phenol rearrangement leads to two isomeric products to which are assigned the 1-acetoxy-4-methyl- (XIX) and 2-acetoxy-4-methyl-(XXIb)-5,6-dihydrobenzo(c)phenanthrene structures, resulting from methylene and methyl migration, respectively. The structure of the 2-acetoxy derivative was proved by dehydrogenation to the fully aromatic 2-hydroxy-4-methylbenzo(c)-phenanthrene (XXII) and independent synthesis of the latter. Reaction mechanisms are considered to account for these observations.

The term "dienone–phenol rearrangement" was coined[2] to encompass not only reactions exemplified by the then well-known[3] rearrangement of santonin (I) to desmotroposantonin (II) but also mechanistically related rearrangements of semibenzenes[4] and quinols.[5] The synthesis[2] of the chrysene dienone III as well as that of its dehydrogenated rearrangement product IV afforded an additional authenticated case of such a methyl migration and thus served as strong support for the 1-methyl-3-hydroxy structure VI proposed for the rearrangement products of steroidal 1,4-dien-3-ones V.[6]



I II



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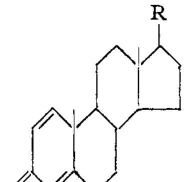

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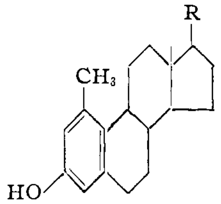
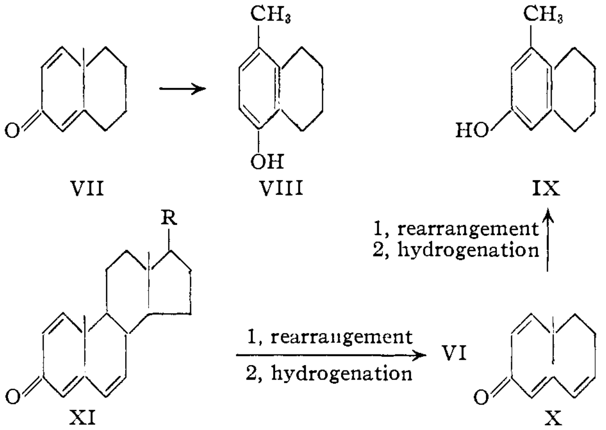


VI

That the dienone–phenol rearrangement can proceed in two directions was demonstrated subsequently by Woodward and Singh[7] who observed that acid-catalyzed rearrangement of the naphthalenic dienone VII proceeded by migration of the methylene rather than angular methyl group to produce 1-methyl-4-hydroxy-5,6,7,8-tetrahydronaphthalene (VIII) rather than the expected 1-methyl-3-hydroxy derivative IX. This in turn suggested that the rearrangement products of steroidal dienones (V) are either the 1-methyl-4-hydroxy or 1-hydroxy-4-methyl isomers and recent dehydrogenation studies[8] have proved conclusively that the latter structure is correct.



The authentic 1-methyl-3-hydroxyphenols (VI) in the steroid series are produced[9] on acid-catalyzed rearrangement of 1,4,6-trien-3-ones XI (followed by hydrogenation of the 6,7-double bond) and the correctness of these structure assignments was supported by similar experiments[10] in the naphthalene series (X → IX). It is clear, therefore, that depending upon the nature of the dienone *under the experimental conditions employed* (acetic anhydride containing a small amount of sulfuric or *p*-toluenesulfonic acid)[11] the dienone–phenol rearrangement can proceed by migration either of the angular methyl group or of one of the methylene groups forming the second ring. As pointed out by

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[1] Monsanto Predoctorate Research Fellow in Organic Chemistry, 1952–1953.

[2] A. L. Wilds and C. Djerassi, THIS JOURNAL, **68**, 1715 (1946).

[3] G. R. Clemo, R. D. Haworth and E. Walton, *J. Chem. Soc.*, 1110 (1930). *Cf.* Huang-Minlon, C. Lo and L. J. Chu, THIS JOURNAL, **65**, 1780 (1943).

[4] K. v. Auwers and K. Ziegler, *Ann.*, **425**, 217 (1921).

[5] E. Bamberger and A. Rising, *Ber.*, **33**, 3636 (1900); E. Bamberger and F. Brady, *ibid.*, **33**, 3642 (1900).

[6] *Inter alia*, H. H. Inhoffen, *et al.*, *Angew. Chem.*, **59**, 207 (1947); *Ann.*, **563**, 127 (1949); *Ber.*, **86**, 116 (1953); C. Djerassi, *et al.*, THIS JOURNAL, **68**, 1712, 2125 (1946); **69**, 2404 (1947); **70**, 1911 (1948); *J. Org. Chem.*, **13**, 697, 848 (1948).

[7] R. B. Woodward and T. Singh, THIS JOURNAL, **72**, 494 (1950).

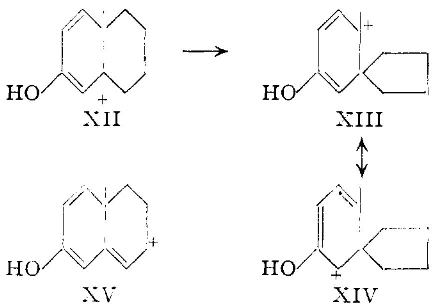
[8] (a) A. S. Dreiding and A. J. Tomasewski, Abstracts, p. 82K, A. C. S. Meeting, Milwaukee, Wis., April 2, 1952; (b) R. B. Woodward, H. H. Inhoffen, H. O. Larson and K. H. Menzel, *Ber.*, **86**, 594 (1953).

[9] C. Djerassi, G. Rosenkranz, J. Romo, J. Pataki and St. Kaufmann, THIS JOURNAL, **72**, 4540 (1950). An independent proof of structure has been presented recently by A. S. Dreiding and W. J. Pummer, *ibid.*, **75**, 3162 (1953).

[10] A. Sandoval, L. Miramontes, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 990 (1951).

[11] The rearrangement may proceed in a different direction with aqueous mineral acid (A. S. Dreiding, W. J. Pummer and A. J. Tomasewski, *ibid.*, **75**, 3159 (1953)).

Woodward and Singh,[7] simple dienones (*e.g.*, V, VII) presumably undergo a Wagner–Meerwein rearrangement to spiran intermediates (XII → XIII → XIV), the structure of the ultimate product being governed in the absence of any other factors by the relative migration aptitudes of the alkyl groups forming the spiran system.[12] On the other hand, when an additional double bond or aromatic ring is placed in conjugation with the dienone grouping (*e.g.*, III, X, XI), conventional[13] methyl migration obtains[9,10] since that additional double bond permits contributing species to the resonance hybrid where the 5,6-bond (steroid numbering system in XI) will acquire some double bond character (*cf.* XV). It appeared of considerable interest to examine the course of a dienone–phenol rearrangement in which the relative importance of contributing species such as XV would be reduced by other factors. The example chosen in the present investigation was the dienone XVIII in the benzo(c)phenanthrene series since the steric interference between the 1- and 12-positions[14] might tend to reduce the importance of carbonium ion intermediates which involve a 12b,12c-double bond (requiring coplanarity) and it thus appeared possible to assess the importance of steric *vs.* electronic factors.



The required dienone XVIII was synthesized by the method developed[2] for the analogous chrysene derivative III. 3-Hydroxymethylene-4-keto-1,2,3,4-tetrahydrophenanthrene (XVI)[15,16] was treated in benzene solution in the presence of sodium hydride[17] with an excess of methyl iodide and the neutral reaction products were separated by chromatography on silica gel.[18] The main product was the desired 3-methyl-3-formyl-4-ketotetrahydrophenanthrone (XVIIa) which was obtained as an oil and identified by the absence of color production with ferric chloride and the smooth cleavage to the known[19,20] 3-methyl-4-ketotetrahydrophenanthrene (XVIIb). The other two substances isolated from the reaction mixture were the cleavage product XVIIb and the known[15] O-alkylation product, 3-methoxymethylene-4-ketotetrahydrophenanthrene; as expected,[2] this gave a slowly developing color with ferric chloride. Condensation of the formyl ketone XVIIa with acetone furnished the crystalline dienone XVIII, the structure of which was supported by its infrared and ultraviolet absorption spectrum. As shown in Fig. 1, the ultraviolet absorption spectra of the dienone XVIII and the unsaturated ketone XXIII (*vide infra*) closely resemble that of 1-naphthalacetone. The spectrum of the corresponding chrysene dienone III is given for comparison and its similarity to 2-naphthalacetone has already been commented upon.[21]

Application of the standard dienone–phenol rearrangement conditions to the dienone XVIII afforded in high yield a *mixture* of two isomers in marked contrast to the previously described dienone–phenol rearrangements[2,6,7,9,10,13] which consistently yielded only *one product* with acetic anhydride–sulfuric acid.[11] The mixture could be separated fairly readily, though inefficiently, by fractional crystallization and afforded two crystalline, isomeric acetates of the empirical formula $C_{21}H_{18}O_2$ with m.p. 133 and 176°, respectively. The absence of polymorphism was established by the marked difference of the infrared spectra, while the practical coincidence of their ultraviolet absorption spectra (Fig. 2) indicated that they must possess essentially the same chromophoric system. The structure of the lower melting acetate (m.p. 133°) was established as that of 2-acetoxy-4-methyl-5,6-dihydrobenzo(c)phenanthrene (XXIb) by the following sequence. Dehydrogenation of the acetate proceeded smoothly to yield the fully aromatic derivative XXIIb and then upon hydrolysis the 2-hydroxy-4-methylbenzo(c)phenanthrene (XXIIa). The latter was synthesized from the 3-carbomethoxy-4-ketotetrahydrophenanthrene (XXV)[20] by the method employed earlier[2] for the preparation of the chrysene derivative IV, *viz.*, Michael condensation with 3-penten-2-one, alkaline cyclization of the intermediate condensation product XXIV (which was not isolated) and finally low-temperature dehydrogenation of the resulting 2-keto-4-methyl-2,3,4,4a,5,6-hexahydrobenzo(c)phenanthrene (XXIII) in *p*-cymene solution to the phenol XXIIa. Identity was established by infrared and mixture melting point comparison of the free phenols as well as of their acetates.

The structure of the lower melting and predominant product from the dienone–phenol rearrangement of the dienone XVIII having been established, it will now be necessary to consider a reasonable formulation for the other isomer (m.p. 176°). Model experiments with 1-methyl-3-acetoxy-11,12-

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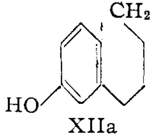
[12] The possibility that the 1,3-shift leading to VIII is the result of electrophilic attack by an intermediate such as XIIa is not excluded.[7,8b]



XIIa

[13] R. T. Arnold, J. S. Buckley and J. Richter, THIS JOURNAL, **69**, 2322 (1947).

[14] *Cf.* M. S. Newman and W. B. Wheatley, *ibid.*, **70**, 1913 (1948); M. S. Newman, and M. Wolf, *ibid.*, **74**, 3225 (1952); W. Theilacker and F. Baxmann, *Ann.*, **581**, 117 (1953); and references cited therein.

[15] K. Meyer and T. Reichstein, *Pharm. Acta Helv.*, **19**, 128 (1944).

[16] W. S. Johnson and W. E. Shelberg, THIS JOURNAL, **67**, 1745 (1945).

[17] Model experiments with the crystalline (ref. 2) 2-methyl-2-formyl-1-ketotetrahydrophenanthrene demonstrated the superiority of sodium hydride over the earlier employed sodium methoxide.

[18] Alumina was completely unsuitable since cleavage of the formyl group was observed.

[19] R. D. Haworth, *J. Chem. Soc.*, 1125 (1932).

[20] W. E. Bachmann and G. D. Cortes, THIS JOURNAL, **65**, 1329 (1943).

[21] A. L. Wilds, L. W. Beck, W. J. Close, C. Djerassi, J. A. Johnson, T. L. Johnson and C. H. Shunk, *ibid.*, **69**, 1985 (1947).

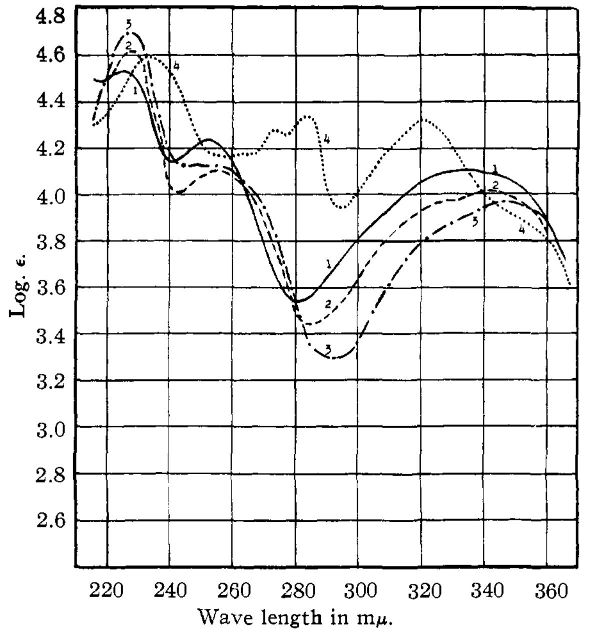


Fig. 1.—Ultraviolet absorption spectra in 95% ethanol: (1) 1-naphthalacetone; (2) 2-keto-4-methyl-2,3,4,4a,5,6-hexahydrobenzo(c)phenanthrene (XXIII); (3) 2-keto-4a-methyl-2,4a,5,6-tetrahydrobenzo(c)phenanthrene (XVIII); (4) 3-keto-12a-methyl-3,11,12,12a-tetrahydrochrysene (III).

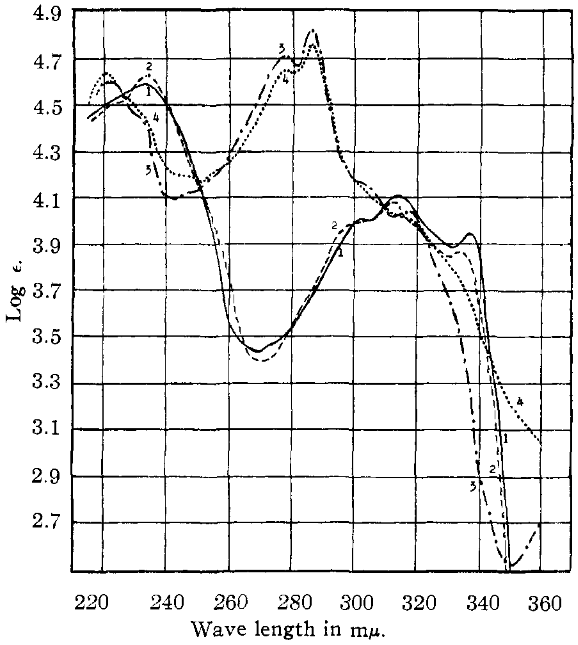
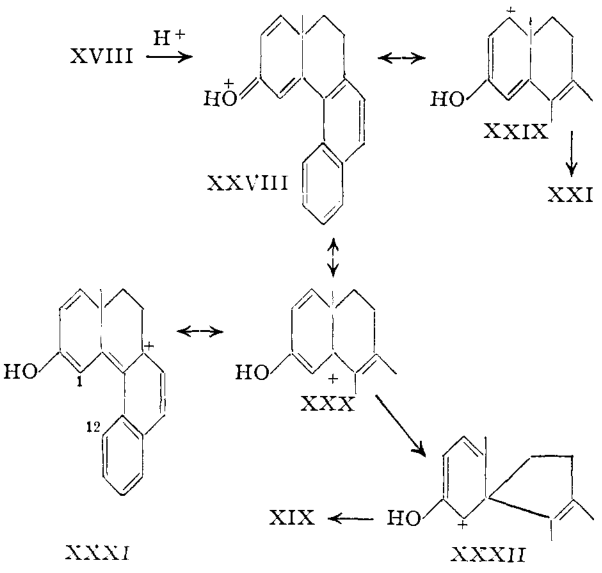
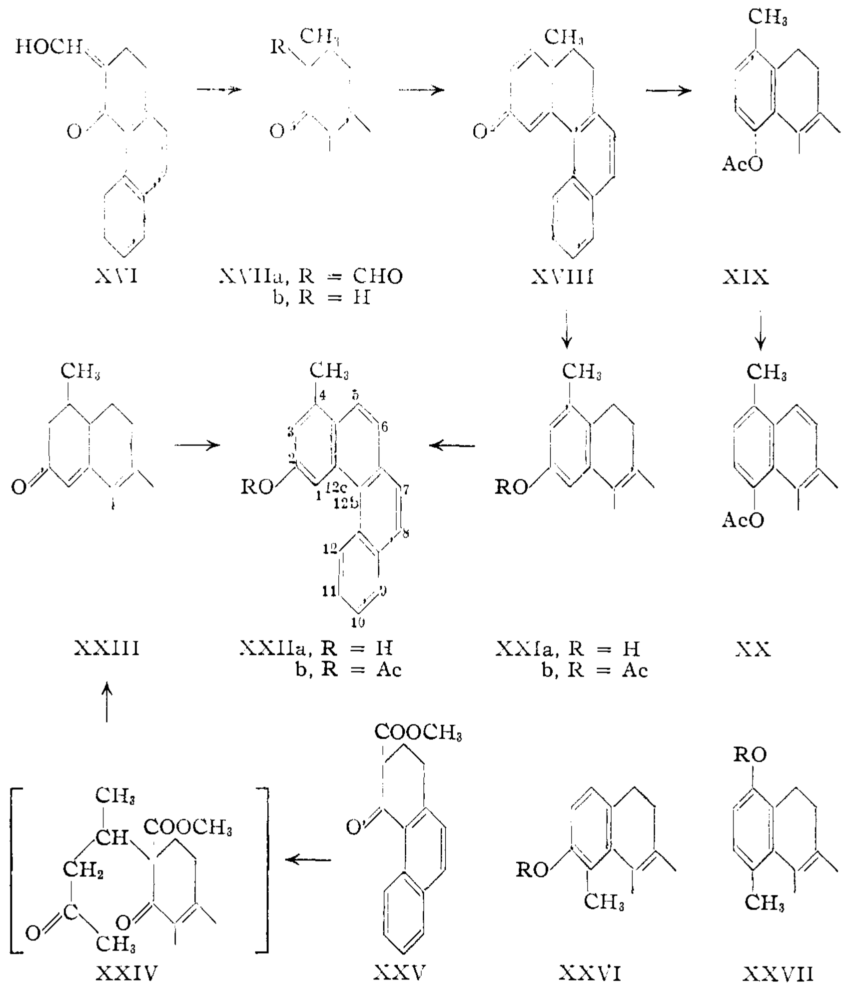


Fig. 2.—Ultraviolet absorption spectra in 95% ethanol: (1) 2-acetoxy-4-methyl-5,6-dihydrobenzo(c)phenanthrene (XXIb); (2) 1-acetoxy-4-methyl-5,6-dihydrobenzo(c)phenanthrene (XIX); (3) 2-acetoxy-4-methylbenzo(c)phenanthrene (XXIIb); (4) 1-acetoxy-4-methylbenzo(c)phenanthrene (XX).

dihydrochrysene, the immediate rearrangement product of the chrysene dienone III, showed that it was very readily hydrolyzed by placement on a weakly alkaline alumina column and that the eluted material was essentially pure phenol. The same behavior was anticipated from the equally unhindered phenolic acetate XXIb in the benzo(c)phenanthrene series and this indeed proved to be the case. However, similar treatment of the m.p. 176° acetate from the acid-catalyzed rearrangement of the dienone XVIII resulted in predominant recovery of unchanged acetate and advantage was taken of this remarkable difference in devising a scheme for the partial separation of the two isomeric rearrangement products which were formed in the approximate ratio of 1(XIX): 2(XXI). Thus, when the crude dienone–phenol rearrangement mixture was passed in petroleum ether–benzene solution through an alumina column, the initially eluted material proved to be the "isoacetate" (m.p. 176°) while continued elution with a more polar solvent produced the dihydrophenol XXIa, which upon acetylation yielded the previously isolated acetate XXIb of m.p. 133°. Hydrolysis of the "isoacetate" (m.p. 176°) yielded the free phenol, which resisted attempts at crystallization but reacetylation regenerated the original, crystalline acetate for which we favor the 1-acetoxy-4-methyl structure XIX, although this has not been proved by synthesis. Dehydrogenation of the isoacetate XIX in the manner employed successfully in the isomeric 2-acetoxy-4-methyl case (XXI → XXII) again led to oily material but the success of the dehydrogenation was established by ultraviolet and infrared measurements. The striking similarity (Fig. 2) of the ultraviolet absorption spectra of the isomeric dihydroacetates (XIX and XXIb) as well as that of their fully dehydrogenated analogs (XX and XXII) constitutes good evidence that the "iso"-series (presumably XIX and XX) contains the unchanged benzo(c)phenanthrene skeleton. The structural possibilities can be reduced further by taking into account the somewhat hindered nature of the phenolic group and by a consideration of the reaction mechanism along the lines employed by Woodward and Singh[7] with the naphthalenic dienone VII.



The conjugate acid XXVIII of the dienone XVIII can give rise to various carbonium ions which for



the sake of simplicity will be considered as separate entities. Of these, XXIX will give rise directly by methyl migration to the 2-acetoxy-4-methyl derivative XXIb of proved constitution. In the chrysene series III, this is the exclusive course of the reaction,[2] because there are no other factors to counteract the distribution of the positive charge through the aromatic rings (analogous to XXXI) and, as has been pointed out earlier,[7] the net effect is thus to confer appreciable double bond character upon the 4a–4b bond and to decrease the probability of methylene migration. However, in the presently considered benzo(c)phenanthrene case, the tertiary (benzyl) carbonium ion (XXX) is probably of considerably greater importance than form XXXI (and the four other species with the positive charge distributed throughout the naphthalene system) since there is some steric inhibition to the required coplanarity in XXXI, etc., due to the interference of the hydrogen atoms at C-1 and C-12. As a result, further changes involving such an intermediate carbonium ion XXX must be considered seriously. One possibility is a twofold migration of the angular methyl group leading ultimately to 1-methyl-2-acetoxy-5,6-dihydrobenzo(c)phenanthrene (XXVI), the phenolic group of which could conceivably be more hindered than that of XXI and thus be in accord with our present observations.

Unless there are certain subtle and unrecognized factors operating in the benzo(c)phenanthrene series, it is much more likely that initial migration of the methylene group occurs to give a spiran intermediate XXXII. While theoretically two products can arise from XXXII, depending on whether the aromatic ring or the methylene group satisfies the adjacent cationoid center, the former would be expected to migrate on the basis of the known preferred migration aptitude of an aromatic ring over an alkyl group. Indeed only the product XIX[22] of the migration of the aromatic ring would be expected to show the resistance to hydrolysis on alumina and with sodium carbonate that is observed experimentally.

It is instructive to note that the over-all energy difference involved in the two reaction sequences apparently is so small that the products of both the migration of the methyl and methylene groups can be formed. It is conceivable that this energy difference could be magnified sufficiently, possibly by the introduction of substituents at the C-12 position, so that the proportion of isomers formed would differ even more markedly.

Experimental[23]

3-Hydroxymethylene-4-keto-1,2,3,4-tetrahydrophenanthrene (XVI).—This substance was prepared in 91% yield by the method of Johnson and Shelberg.[16] Except for the first run when a m.p. of 39.4–40° was observed, in agreement with the literature values,[15,16] in all subsequent experiments even the crude material exhibited m.p. 49–50°, which was raised on recrystallization from ether–pentane to m.p.

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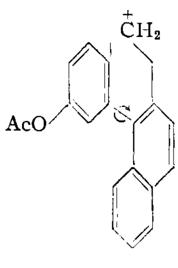
[22] The other product would be 1-methyl-4-acetoxy-5,6-dihydrobenzo(c)phenanthrene (XXVII), which is not excluded as the correct structure of the "isoacetate" obtained from the dienone–phenol rearrangement of XVIII. However, one would not expect, *a priori*, any particular difference in the behavior of XXI and XXVII on basic hydrolysis. The 4-acetoxy derivative could be formed by an alternate mechanism (*cf.* ref. 7, 8b) involving electrophilic attack by an intermediate such as XXXIII, but there seems to be little reason to invoke such a mechanism (since it would also be operative in the chrysene series (ref. 2) where no product of such a rearrangement was isolated) unless the governing factor is the placement of the least bulky group at the C-1 position.



XXXIII

[23] Melting points are uncorrected. We are indebted to Mr. M. Papo and Miss Phyllis Tocco for the microanalyses. Infrared spectra were measured with a Baird Associates recording double beam infrared spectrophotometer in 0.1-mm. cells.

50–51° (vac.), immediate dark blue color with ferric chloride, $\lambda_{max}^{CHCl_3}$ 6.11, 6.19 and 6.25 μ (of almost equal intensity).[24] By comparison, 4-ketotetrahydrophenanthrene shows an intense band at 6.02 μ, while the double bond peaks at 6.18 and 6.25 μ are of only medium intensity. It is evident that the material of m.p. 50–51° represents a higher melting polymorphic form of XVI.

Anal. Calcd. for $C_{15}H_{12}O_2$: C, 80.33; H, 5.39. Found: C, 80.59; H, 5.52.

3-Methyl-3-formyl-4-keto-1,2,3,4-tetrahydrophenanthrene (XVIIa).—A solution of 13.44 g. of 3-hydroxymethylene-4-ketotetrahydrophenanthrene (XVI) in 150 cc. of dry benzene was added to a suspension of 1.44 g. of sodium hydride in 250 cc. of benzene. After stirring and refluxing for 1.5 hours in an atmosphere of nitrogen, the suspension of the yellow enolate was cooled, 60 cc. of methyl iodide in 100 cc. of dry benzene was added and refluxing with constant stirring in an atmosphere of nitrogen was continued for 68 hours. Additional amounts of methyl iodide were added after the twentieth (40 cc.) and forty-second hour (30 cc.). At the end of the reflux period, methanol was added to destroy the excess sodium hydride, the mixture was poured into ice-water and extracted thoroughly with ether. The organic layer was washed several times with ice-cold 5% potassium hydroxide solution, water, dried and evaporated leaving 11.75 g. of oil. This oil was treated with Norit in ether solution and after concentration and dilution with pentane yielded (in two crops) 1.62 g. of yellowish **3-methoxymethylene-4-keto-1,2,3,4-tetrahydrophenanthrene** with m.p. 106–110°, which together with the material isolated below in the chromatogram amounted to 27% of O-alkylation product. Recrystallization from 95% ethanol raised the melting point of the yellowish needles to 112.5–114° (lit.[15] m.p. 114°), $\lambda_{max}^{CHCl_3}$ 5.99, 6.30, 8.03 and 8.73 μ. The usual double bond peaks at 6.16 and 6.24 μ were much more intense than in XVIIa and XVIIb. The pronounced infrared maxima at 8.03 and 8.73 μ, not found in the C-alkylation product XVIIa or the cleavage product XVIIb, together with the *slowly developing* (15 minutes) color with ferric chloride, served to distinguish the O-ether from the other compounds.

Evaporation of the combined mother liquors gave an oil which still exhibited a slowly developing color with ferric chloride indicating the presence of some O-ether and it was, therefore, chromatographed in benzene solution on 930 g. of silica gel (28–200 mesh, previously washed with benzene).[25] The initially eluted, crystalline fractions (m.p. range 57–63°) amounted to 1.36 g. (11%) and were identified as the cleavage product **3-methyl-4-keto-1,2,3,4-tetrahydrophenanthrene** (XVIIb) by infrared comparison (see below).

The second, major fraction, also eluted with benzene, yielded 6.15 g. (43%) of a pinkish oil, which resisted all attempts at crystallization. The cleavage (see below) to the 3-methyl-4-ketone XVIIb and the infrared spectrum ($\lambda_{max}^{CHCl_3}$ 5.77 (aldehyde) and 5.99 μ (conjugated ketone) of equal intensity) indicated that this was essentially pure **3-methyl-3-formyl-4-keto-1,2,3,4-tetrahydrophenanthrene** (XVIIa) and this was employed in the next step. The substance seems to be stable as shown by infrared examination after 7 months storage.

The ultimately eluted (benzene–ether and pure ether) material (2.26 g.) was shown by infrared analysis to consist chiefly of the O-ether contaminated with a small amount of the C-alkylation product XVIIa.

Cleavage of 3-Methyl-3-formyl-4-ketotetrahydrophenanthrene (XVIIa) to 3-Methyl-4-ketotetrahydrophenanthrene (XVIIb).—A solution of 0.235 g. of the formyl ketone XVIIa in 9 cc. of petroleum ether–benzene (1:2) was placed on 7 g. of activated alumina (activity II, *p*H 8–9) and eluted after 17 hours; yield 135 mg. (66%), m.p. 60–62°. Recrystallization from ethanol gave colorless plates of the cleavage product XVIIb with m.p. 66.5–68°, $\lambda_{max}^{CHCl_3}$ 5.97 μ; lit.[19,20] m.p. 64–66°.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.45; H, 7.09.

2-Keto-4a-methyl-2,4a,5,6-tetrahydrobenzo(c)phenanthrene (XVIII).—A mixture of 3.35 g. of chromatographically-purified 3-methyl-3-formyl-4-ketotetrahydrophenanthrene (XVIIa), 50 cc. of dry acetone, 0.875 g. of glacial acetic acid and 0.625 g. of piperidine (dried over sodium) was refluxed for 59 hours in an atmosphere of nitrogen, an additional 0.650 g. of acetic acid and 0.425 g. of piperidine having been added after the first 24 hours. Most of the solvent was removed on the steam-bath, benzene–ether was added and the solution was washed until neutral, dried and evaporated. Just as in the chrysene series,[2] the intermediate 3-methyl-3-(1′-hydroxy-3′-ketobutyl)-4-ketotetrahydrophenanthrene was oily and the entire material (3.52 g.) in 60 cc. of methanol was cyclized by refluxing for 6 hours with 6 cc. of 45% potassium hydroxide solution in an atmosphere of nitrogen. After working up in the usual way by ether–benzene extraction, the oily residue was crystallized from ether to yield in two crops 0.67 g. of the desired dienone XVIII with m.p. 156–158°.

The combined mother liquors were chromatographed on 85 g. of ethyl acetate-washed alumina (activity II) and yielded from the petroleum ether–benzene (2:1) eluates 1.53 g. (52%) of 3-methyl-4-ketotetrahydrophenanthrene (XVIIb) with m.p. 60–65° and identified by infrared comparison. From the benzene and benzene–ether (9:1) eluates there was isolated an additional 0.32 g. of dienone XVIII with m.p. 153–158°, thus raising the yield of this material to 27%. The analytical sample was prepared by recrystallization from ethyl acetate and sublimation at 140° and 0.01 mm., m.p. 164–165° (cor.), $\lambda_{max}^{CHCl_3}$ 6.04, 6.20 and 6.30 μ, λ_{max}^{EtOH} 228, 244–253 (plateau) and 346 mμ (log ε 4.69, 4.13, 3.97) and minimum at 292.5 mμ (log ε 3.30) (*cf.* Fig. 1).

Anal. Calcd. for $C_{19}H_{18}O$: C, 87.66; H, 6.20. Found: C, 87.38; H, 6.34.

From a preparative standpoint, it was preferable to avoid the isolation of the intermediate formyl ketone XVIIa. Thus the crude reaction product (11.29 g.) obtained from the methylation of 11.2 g. of hydroxymethylene ketone (XVI) upon condensation with acetone in the above described manner yielded 3.0 g. (23% over-all yield based on XVI) of the dienone XVIII as well as 39% of 3-methyl-4-ketotetrahydrophenanthrene (XVIIb) and 13% of 4-ketotetrahydrophenanthrene (presumably arising from cleavage of the 3-methoxymethylene-4-keto derivative).

Dienone–Phenol Rearrangement of 2-Keto-4a-methyl-2,4a,5,6-tetrahydrobenzo(c)phenanthrene (XVIII).—To a cold solution of 0.475 g. of the above dienone XVIII in 20 cc. of acetic anhydride was added 80 mg. of sulfuric acid dissolved in 2 cc. of acetic anhydride. After 4.5 hours at room temperature, the initial red coloration had turned to yellow and the entire reaction mixture was diluted with ice-water. The product was extracted with ether, washed, dried and evaporated, leaving a nearly colorless paste which upon trituration with ether furnished 80 mg. of colorless crystals with m.p. 170–172°. Recrystallization from ethanol afforded needles of **1-acetoxy-4-methyl-5,6-dihydrobenzo(c)-phenanthrene (XIX)** with m.p. 175–176°, ultraviolet absorption spectrum in Fig. 2, $\lambda_{max}^{CHCl_3}$ 5.70 μ (phenolic acetate) and characteristic band at 12.24 μ.

Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00. Found: C, 83.28; H, 5.68.

Concentration of the original ether solution and chilling produced 85 mg. of crystals with m.p. 130–131°, which after recrystallization from ethanol furnished the analytical sample of **2-acetoxy-4-methyl-5,6-dihydrobenzo(c)phenanthrene** (XXIb) as small prisms with m.p. 132–133°, $\lambda_{max}^{CHCl_3}$ 5.70 and 12.24 μ (but strikingly different in the "finger-print" region from that of XIX), ultraviolet absorption spectrum in Fig. 2. A mixture of XIX and XXIb melted at 120–140°.

Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00. Found: C, 83.54; H, 5.82.

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[24] No free hydroxyl absorption was noted in the 3 μ region, an observation in accord with that of G. N. Walker (THIS JOURNAL, **75**, 3393 (1953)) with other hydroxymethylene ketones where the absence of hydroxyl absorption is attributed to chelation.

[25] Preliminary model experiments for evaluating the optimum adsorbent were carried out with the crystalline 2-methyl-2-formyl-1-keto-1,2,3,4-tetrahydrophenanthrene (ref. 2). Thus, 100 mg. of the formyl ketone (m.p. 107–108.5°) after chromatography on 8 g. of silica gel furnished 80 mg. of pure formyl ketone (m.p. 108–109°) and 20 mg. of impure material (m.p. 100–104°). On the other hand, a similar chromatogram, but employing ethyl acetate-washed alumina (*p*H 7–8) gave 98% of the crude cleavage product 2-methyl-1-keto-tetrahydrophenanthrene with m.p. 61–68°, raised after one recrystallization to 70–72°.

In order to devise a more effective means of separation of the two isomeric acetates (XIX and XXIb), 30 mg. each of the following pure compounds was chromatographed individually on 3.0 g. of ethyl acetate-washed alumina (activity II, *p*H 7–8) in petroleum ether–benzene (9:1) solution, the chromatograms being developed only after 12 hours standing.

3-Acetoxy-1-methyl-11,12-dihydrochrysene[2] (m.p. 121–122°), the rearrangement product of the chrysene dienone III, yielded 22 mg. of 3-hydroxy-1-methyl-11,12-dihydrochrysene[2] with m.p. 189–191°.

2-Acetoxy-4-methyl-5,6-dihydrobenzo(c)phenanthrene (XXIb) (m.p. 131–133°) afforded 22 mg. of **2-hydroxy-4-methyl-5,6-dihydrobenzo(c)phenanthrene** (XXIa) with m.p. 155–157°, indicating nearly complete cleavage. The free phenol XXIa was most conveniently prepared by adding an ethereal solution of 100 mg. of the acetate XXIb to a mixture of 100 mg. of lithium aluminum hydride in ether and stirring for 30 minutes at room temperature. After working up in the usual manner, the phenol XXIa was isolated in nearly quantitative yield; m.p. 156–157° (after crystallization from ether–pentane), $\lambda_{\max}^{CHCl_3}$ 2.75 and 3.0 μ (broad), but no band in the 5–6 μ region; the band at 12.24 μ, found in the various 5,6-dihydrobenzo(c)phenanthrenes, also was present.

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.66; H, 6.19. Found: C, 87.44; H, 6.28.

1-Acetoxy-4-methyl-5,6-dihydrobenzo(c)phenanthrene (**XIX**) (m.p. 175–176°) gave 60% of recovered acetate (m.p. 168–170°) after remaining on the column for 12 hours. The rest of the material was eluted with benzene–ether (10 mg.) and showed only hydroxyl absorption ($\lambda_{\max}^{CHCl_3}$ 2.75 μ) in the infrared. It is interesting to note that the band at 3.0 μ (presumably due to a bonded OH-group) found in XXIa was absent in this instance. It was not possible to crystallize this phenol and a similar observation was made when a larger sample of the acetate XIX was treated with lithium aluminum hydride. The phenol obtained in nearly quantitative yield, exhibited the proper infrared spectrum and upon reacetylation with acetic anhydride–pyridine regenerated the original, crystalline acetate XIX.

On the basis of the above three chromatogram experiments, it is clear that the 2-acetoxy derivative XXIb is cleaved nearly quantitatively as is the case in the chrysene series, while the 1-acetoxy isomer XIX is cleaved only to the extent of *ca.* 40%.

In order to demonstrate that this above difference in the behavior of the two isomeric acetates on alumina is a true reflection of the above hindered character of the phenolic group in XIX rather than purely an adsorption phenomenon, 25 mg. of each acetate in 25 cc. of 95% ethanol was treated at room temperature for 35 minutes with 19 mg. of sodium carbonate in 5 cc. of water. After processing in the usual manner, the crystalline isoacetate XIX was recovered in *ca.* 75% yield while the acetate XXIb suffered hydrolysis to the extent of *ca.* 80%.

Taking advantage of the observed difference of the two substances, both in terms of solubility as well as reactivity toward alumina, the following experiment was carried out to determine the relative amounts formed of the two rearrangement products. The dienone XVIII (3.32 g.) on rearrangement in the above indicated manner furnished 3.17 g. of nearly colorless solid, m.p. 107–115°, and an additional 1.0 g. of pasty material. Both fractions were combined and crystallized from ether (with seeding) yielding first 0.28 g. of isoacetate XIX with m.p. 173–175° and then 0.49 g. of 2-acetoxy-4-methyl derivative XXIb (m.p. 131–133°). Chromatography of the combined mother liquors on ethyl acetate-washed alumina furnished 0.32 g. of crude isoacetate (0.22 g. of pure material) in the petroleum ether–benzene eluates and 2.35 g. of crude phenol (absence of acetate band in infrared) with m.p. 125–157° in the benzene–ether fractions. Reacetylation of the phenolic material and recrystallization gave an additional 0.85 g. of XXIb and 0.05 g. of XIX making a total of 1.34 g. of pure 2-acetoxy-4-methyl-(XXIb) and 0.55 g. of pure 1-acetoxy-4-methyl-(XIX) 5,6-dihydrobenzo(c)phenanthrene.

2-Keto-4-methyl-2,3,4,4a,5,6-hexahydrobenzo(c)phenanthrene (**XXIII**).—Since attempts to effect the condensation of 3-penten-2-one with 3-hydroxymethylene-4-ketotetrahydrophenanthrene (XVI) failed,[26] we resorted to the method employed successfully in the chrysene series.[2]

After refluxing a solution of 0.76 g. of 3-carbomethoxy-4-ketotetrahydrophenanthrene (XXV),[20] 0.047 g. of sodium methoxide, 12 cc. of benzene and 2 cc. of methanol for 10 minutes in an atmosphere of nitrogen, the mixture was cooled and let stand at room temperature for 42 hours with 1 cc. of freshly distilled 3-penten-2-one. The dark red solution was acidified with dilute acetic acid, ether was added and the organic layer was washed until neutral, dried and evaporated. The crude condensation product (XXIV) was cyclized directly by refluxing in a nitrogen atmosphere for 47 hours with 100 cc. of 5% aqueous potassium hydroxide solution. The product was extracted with hot benzene, washed until neutral, dried, evaporated and crystallized from ether yielding 0.24 g. of the desired ketone XXIII with m.p. 129–134°. Further recrystallization from ethyl acetate furnished the analytical sample as stout prisms with m.p. 133.5–134.5°; $\lambda_{\max}^{CHCl_3}$ 6.02 and 6.28 μ; the ultraviolet absorption spectrum (Fig. 1) closely resembled that of 1-naphthalacetone.[21]

Anal. Calcd. for $C_{19}H_{18}O$: C, 86.98; H, 6.91. Found: C, 86.93; H, 7.15.

2-Hydroxy-4-methylbenzo(c)phenanthrene (**XXII**). (a) By **Dehydrogenation** of **2-Acetoxy-4-methyl-5,6-dihydrobenzo(c)phenanthrene** (**XXIb**).—A mixture of 0.40 g. of the dihydroacetate XXIb and 0.16 g. of 5% palladized charcoal was heated in an atmosphere of nitrogen at 210–240° for 10 minutes followed by 15 minutes at 260–270°. Benzene was added, the catalyst was filtered, the benzene was evaporated and the residue was reacetylated by treatment with acetic anhydride–pyridine for 12 hours. After processing the reaction mixture in the usual manner, there was obtained 0.37 g. (93%) of colorless crystals with m.p. 148–153°. Recrystallization from ethanol yielded long, silky needles (0.3 g.) of the **acetate XXIIb** with m.p. 164–165.5°. $\lambda_{\max}^{EtOH}$ 220, 278, 286 and 317 mμ (log ϵ 4.60, 4.70, 4.82, 4.05) (*cf.* Fig. 2), $\lambda_{\max}^{CHCl_3}$ 5.70 and 11.95 μ (12.24 μ band of dihydro precursor XXIb absent).[27] Solutions of this substance in organic solvents exhibit strong bluish-violet fluorescence.

Anal. Calcd. for $C_{21}H_{16}O_2$: C, 83.98; H, 5.37. Found: C, 83.64; H, 5.65.

A sample (0.15 g.) of the acetate XXIIb in 25 cc. of ether was added to a suspension of 0.10 g. of lithium aluminum hydride in 45 cc. of the same solvent. After 45 minutes at room temperature, the mixture was worked up in the standard manner and the residue was crystallized from ethyl acetate–pentane; 0.09 g., m.p. 146–147.5°. The analytical sample of the **phenol XXIIa** was sublimed at 120° and 0.005 mm.; colorless crystals, m.p. 148–148.5° (vac.).

Anal. Calcd. for $C_{19}H_{14}O$: C, 88.34; H, 5.46. Found: C, 88.25; H, 5.71.

(b) **By Dehydrogenation of 2-Keto-4-methyl-2,3,4,4a,5,6-hexahydrobenzo(c)phenanthrene** (**XXIII**).—A solution of 0.155 g. of the hexahydroketone XXIII in 2 cc. of *p*-cymene was refluxed for 70 hours with 65 mg. of 5% palladized charcoal in an atmosphere of nitrogen. Addition of ethanol, filtration of the catalyst and evaporation to dryness yielded a semi-solid which was acetylated directly with acetic anhydride–pyridine. Crystallization of the acetylation product from ether furnished 0.08 g. of the **acetate XXIIb** with m.p. 164–164.5° and an additional 0.015 g. melting at 152–154°. Identity of the first crop material with the acetate prepared according to (a) was established by a mixture melting point determination as well as by comparison of the infrared and ultraviolet spectra.

For further confirmation, 40 mg. of the acetate was treated with lithium aluminum hydride as indicated under (a) to furnish 30 mg. of colorless phenol XXIIa with m.p. 145–147° undepressed upon admixture with the phenol synthesized according to (a); the infrared spectra also proved to be identical.

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(26) The corresponding reaction with methyl vinyl ketone is successful and offers a route to 2-substituted benzo(c)phenanthrenes (A. L. Wilds and R. G. Werth, *J. Org. Chem.*, **17**, 1154 (1952)).

(27) A similar dehydrogenation of the "isoacetate" (XIX) gave an oily product, resisting crystallization even after chromatography. The oil thus obtained was essentially the pure benzo(c)phenanthrene XX as indicated by the practical identity of its ultraviolet absorption spectrum ($\lambda_{\max}^{EtOH}$ 221, 277, 286, 316 mμ; log ϵ 4.63, 4.65, 4.75, 4.02) with that of the 2-acetoxy-4-methyl isomer XXIIb (Fig. 2) and by the presence of the characteristic "aromatic" 11.95 μ infrared band and the absence of the 12.24 μ band (present in XIX); the typical fluorescence also was noted.