

the consumption of 1 mole (99.6% of theory). The catalyst was removed by filtration and the filtrate was evaporated. Benzene (50 ml.) was added and evaporated to remove remaining traces of ethanol. The residual oil was used directly without further purification.

To a stirred slurry of 1.9 g. (0.05 mole) of lithium aluminum hydride in 75 ml. of anhydrous ether was slowly added a solution of the hydrogenation product IIb in 25 ml. of ether. The mixture was refluxed with stirring for 2 hr., cooled, and decomposed by the addition of 2 ml. of water, 2 ml. of 25% sodium hydroxide, and 6 ml. of water in that order. The precipitated aluminate

salts were separated by filtration and the filtrate was treated directly with ethereal hydrogen chloride. The precipitated hydrochloride was filtered, washed with ether, and dried. There was obtained 7.3 g. (90.9% for the two steps) of white solid, m.p. 204–205°. Pure V was obtained as a white solid from ethanol-ether; m.p. 213.5–215°. This material was identical in all respects with that prepared in part A.

**Acknowledgment.**—The author is deeply indebted to Paul E. Marlatt for the preparation of sufficient quantities of I to enable this work to be carried out.

[CONTRIBUTION FROM THE EVANS CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY, COLUMBUS 10, OHIO]

## The Synthesis and Ionization Constants of the Six Hydroxybenzo[*c*]phenanthrenes<sup>1</sup>

BY MELVIN S. NEWMAN AND JOCHANAN BLUM<sup>2</sup>

RECEIVED SEPTEMBER 4, 1963

The syntheses of the six hydroxybenzo[*c*]phenanthrenes is described. None of these compounds exists to any detectable extent in an isomeric ketonic form. 1-Hydroxybenzo[*c*]phenanthrene is appreciably weaker as an acid than the other five isomers.

The compound benzo[*c*]phenanthrene (I) and certain of its derivatives have been of interest to us in several connections. Originally, the attempt to correlate the carcinogenic activity of I and of the six monomethyl derivatives of I with some property of the hydrocarbons was of major concern.<sup>3</sup> More recently, interest in the properties of the functional derivatives of I has been of concern because of the steric strains inherent in this polycyclic system.<sup>4</sup> For example, all six of the monocarboxylic acids have been prepared and their ionization constants determined.<sup>5</sup>

In the present study, all of the hydroxy derivatives of benzo[*c*]phenanthrene have been prepared with three objectives in mind: a, to measure the ionization constants; b, to see if any of these compounds might exist partly or totally as an isomeric ketone; and c, to supply compounds for testing of carcinogenic or anticarcinogenic activity.

The ionization constants have been measured and are listed in Table I together with those of a few related compounds.<sup>6</sup> The most noteworthy facts are that 4-phenanthrol and 1-benzo[*c*]phenanthrol are appreciably weaker in acid strength than all of the other phenanthrols and benzo[*c*]phenanthrols. We attribute this to steric hindrance to solvation of the corresponding anions. A similar explanation for the weakness of hindered aliphatic acids has been advanced.<sup>7</sup>

No evidence of a ketonic component has been obtained in any member of this series<sup>8</sup> as judged by the absence of a carbonyl absorption band in the infrared spectra.

The compounds have been sent for testing<sup>9</sup> in the cancer field to Dr. James A. Miller, McArdle Memorial

Laboratory, Madison, Wis. More of each compound is available if there are other persons interested in other measurements.

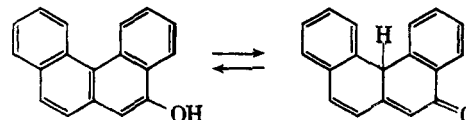
TABLE I  
IONIZATION CONSTANTS OF PHENANTHROLS AND BENZO[*c*]-  
PHENANTHROLS (50% BY WEIGHT ETHANOL)

	p <i>K</i> <sub>a</sub>
2-Phenanthrol	10.50
4-Phenanthrol	11.33
9-Phenanthrol	10.51
Hydroxybenzo[ <i>c</i> ]phenanthrene	
1-	11.31
2-	10.44
3-	10.35
4-	10.56
5-	10.54
6-	10.26

The syntheses of 1-, 2-, and 3-hydroxybenzo[*c*]phenanthrene were accomplished by demethylation of the corresponding methoxy benzo[*c*]phenanthrenes, which were synthesized<sup>10</sup> as shown in the accompanying formulas. Both 2-methoxy and 2-hydroxybenzo[*c*]phenanthrene<sup>11</sup> and 3-methoxybenzo[*c*]phenanthrene<sup>12</sup> have been prepared.

The demethylation of the 2-methoxy and 3-methoxy compounds was accomplished without difficulty, but the demethylation of 1-methoxybenzo[*c*]phenanthrene

(8) It was thought that perhaps isomerization to a ketonic state would relieve part of the steric strain; e.g.



(9) Hydroxybenzo[*c*]phenanthrenes may be of interest as possible metabolic products of the parent hydrocarbon. For references to polycyclic aromatic hydrocarbon metabolites and their possible connection with cancer, see A. Pullman and B. Pullman, *Advan. Cancer Res.*, **3**, 117 (1955); E. Boyland and P. Sims, *Biochem. J.*, **84**, 571 (1962), and references therein. No work in this connection has been carried out with benzo[*c*]phenanthrene to our knowledge.

(10) See M. S. Newman and R. M. Wise, *J. Am. Chem. Soc.*, **78**, 450 (1956), and M. S. Newman and M. Wolf, *ibid.*, **74**, 3225 (1952), for analogous syntheses.

(11) (a) A. L. Wilds and R. G. Werth, *J. Org. Chem.*, **17**, 1154 (1952); (b) J. Szmuszkovicz and E. J. Modest, *J. Am. Chem. Soc.*, **72**, 566 (1950); (c) G. T. Tatevosyan and V. O. Babayan, *Zh. Obshchei Khim.*, **22**, 1421 (1952).

(12) J. Szmuszkovicz and E. J. Modest, *J. Am. Chem. Soc.*, **70**, 2542 (1948).

(1) This work was supported by a grant from the National Institutes of Health.

(2) Postdoctoral Fellow, 1963.

(3) In this connection the following papers are of interest: (a) K. H. Takemura, M. D. Cameron, and M. S. Newman, *J. Am. Chem. Soc.*, **75**, 3280 (1953); (b) M. S. Newman, M. Levy, and M. Szwarc, *ibid.*, **77**, 4225 (1955); (c) M. S. Newman and S. Otsuka, *J. Natl. Cancer Inst.*, **21**, 721 (1958).

(4) The study of the geometry of I and related compounds by X-ray crystallography has been under investigation: see F. H. Herbstein and G. M. J. Schmidt, *J. Chem. Soc.*, 3302 (1954); F. L. Hirshfeld, S. Sandler, and G. M. J. Schmidt, *ibid.*, 2108 (1963).

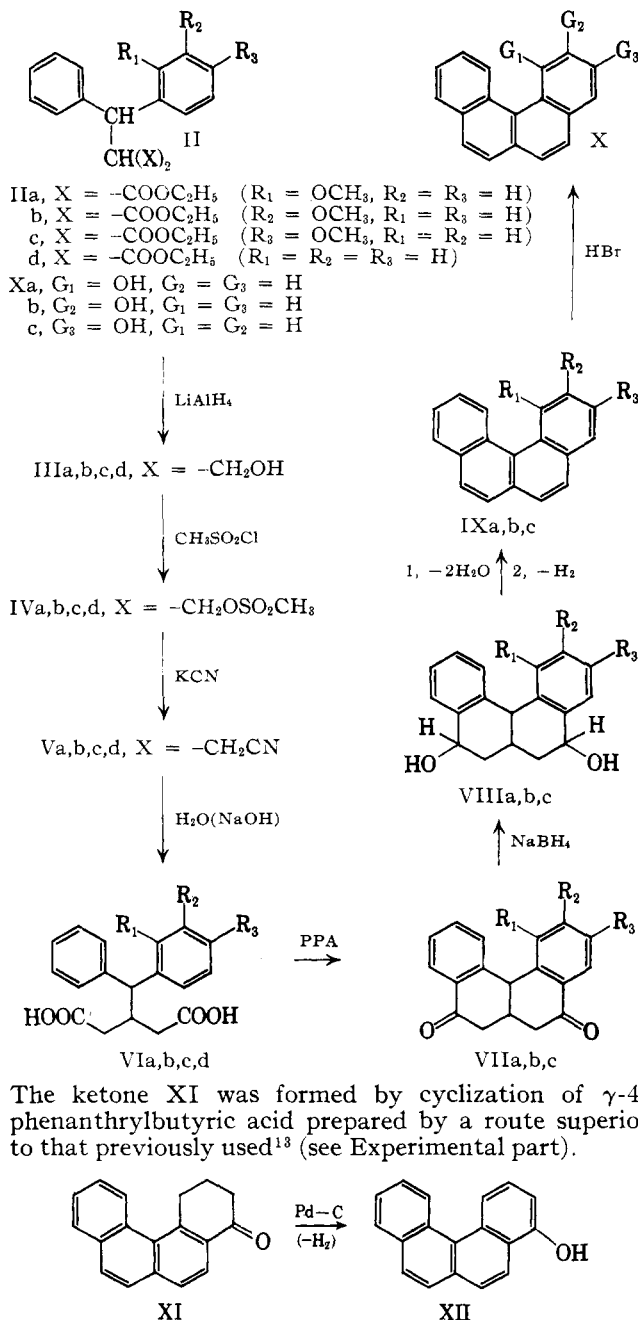
(5) M. S. Newman and H. Boden, *J. Am. Chem. Soc.*, **83**, 115 (1961).

(6) In a private communication, Dr. W. N. White and Mr. H. Rosenberg report that the ionization constants of 2-, 3-, and 9-phenanthrol, 1- and 2-naphthol, and 1- and 2-anthrol in 50% aqueous methanol have p*K*<sub>a</sub> values of 10.02 to 10.22.

(7) G. S. Hammond and D. H. Hogle, *J. Am. Chem. Soc.*, **77**, 338 (1955); M. S. Newman and T. Fukunaga, *ibid.*, **85**, 1176 (1963).

was very sensitive to reaction conditions and could be effected in only moderate yield after many unsuccessful attempts. The difficulty was undoubtedly connected with the strain present in the 1-methoxy and 1-hydroxy compounds.

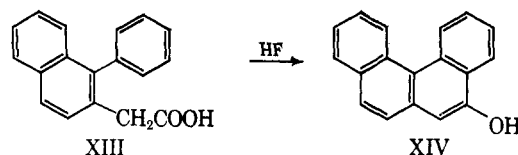
The synthesis of 4-hydroxybenzo[*c*]phenanthrene (XII) was effected in 71% yield by the dehydrogenation of 4-keto-1,2,3,4-tetrahydrobenzo[*c*]phenanthrene (XI) over palladium-on-charcoal in refluxing *p*-cymene.



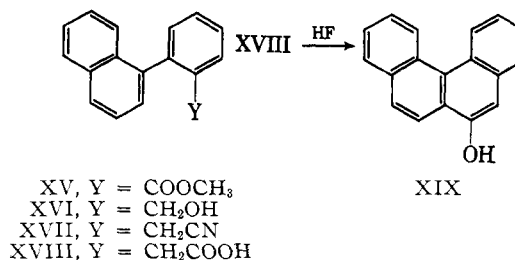
The ketone XI was formed by cyclization of  $\gamma$ -4-phenanthrylbutyric acid prepared by a route superior to that previously used<sup>13</sup> (see Experimental part).

(13) W. E. Bachmann and R. D. Edgerton, *J. Am. Chem. Soc.*, **62**, 2970 (1940).

(14) M. S. Newman and L. M. Joshel, *ibid.*, **62**, 972 (1940).



The synthesis of 6-hydroxybenzo[*c*]phenanthrene (XIX) was accomplished by the cyclization of *o*-(1-naphthyl)-phenylacetic acid (XVIII) with hydrogen fluoride. The requisite acid XVIII was prepared in four steps from methyl *o*-(1-naphthyl) benzoate (XV).



The synthesis of phenolic materials by cyclization of appropriate acids has been accomplished before.<sup>15</sup> The yields in the syntheses of XIV (80%) and XIX (71%) were quite good. Anhydrous hydrogen fluoride was the condensing agent.

#### Experimental<sup>16</sup>

**Diethyl Benzhydrylmalonates (IIa,b,c,d).**—To a well-stirred solution of 65 g. of diethyl benzalmonate<sup>17</sup> in 120 ml. of dry benzene containing 2 g. of cuprous bromide was added the Grignard reagent prepared from 47 g. of *o*-bromoanisole in 120 ml. of ether, the temperature being held at  $-5$  to  $0^\circ$ . After stirring for 10 min. at  $0^\circ$ , the mixture was poured on ice and dilute acid and was worked up in the usual way. Distillation afforded a fraction, b.p.  $218$ – $222^\circ$  at 4 mm., which crystallized on standing. Recrystallization from cyclohexane yielded 56 g. (63%) of IIa as colorless crystals, m.p.  $81.5$ – $82.0^\circ$ .

When the above reaction was carried out without cuprous bromide at  $0$ – $10^\circ$  and at room temperature for 16 hr., no IIa was isolated. Instead a 47% yield of ethyl  $\alpha$ -*o*-methoxybenzoyl- $\beta$ -*o*-methoxyphenyl- $\beta$ -phenylpropionate, b.p.  $208$ – $210^\circ$  at 2.5 mm., was obtained as a pale yellow viscous oil (infrared at 5.80, 5.85, and  $6.05 \mu$ ).

*Anal.* Calcd. for  $\text{C}_{26}\text{H}_{26}\text{O}_5$ : C, 74.7; H, 6.2. Found<sup>m</sup>: C, 74.5; H, 6.2.

In a similar way, a solution of 139 g. of diethyl *m*-methoxybenzalmonate,<sup>19</sup> m.p.  $46.2$ – $47.4^\circ$  (prepared in 94% yield from *m*-methoxybenzaldehyde and ethyl malonate), in 250 ml. of benzene containing 7 g. of cuprous bromide was heated with 0.5 mole of ethereal phenylmagnesium bromide at  $-5$ – $0^\circ$  and then stirred at room temperature for 2 hr. Distillation and redistillation afforded 156 g. (88%) of IIb as a pale yellow viscous oil, b.p.  $178$ – $179^\circ$  at 1 mm.

Similarly, the Grignard reagent from 62 g. of *p*-bromoanisole was added to 85 g. of diethyl benzalmonate<sup>17</sup> in benzene containing 2.5 g. of cuprous bromide. The solution after stirring

(15) H. H. Chatterjee, *J. Indian Chem. Soc.*, **12**, 591 (1935); I. R. Sherwood, W. F. Short, and J. Woodcock, *J. Chem. Soc.*, 322 (1936), prepared 9-phenanthrol from 2-biphenylacetic acid, but no yields were mentioned.

(16) All melting points are uncorrected. The term "worked up in the usual manner" means that an organic solvent solution, usually ether-benzene, 1:1, of the products was washed with acid and/or alkali as indicated, then with saturated sodium chloride solution, then dried by shaking with or filtering through magnesium sulfate. The solvents were then removed and the residue crystallized or distilled. Analyses marked m by Micro-analysis Laboratories, Wilmington, Del., and g by Galbraith Laboratories, Knoxville, Tenn.

(17) C. F. H. Allen and F. W. Spangler, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 377.

(18) Compare G. A. Holmberg, *Acta Chem. Scand.*, **6**, 421 (1952), who prepared IIa, m.p.  $86$ – $87^\circ$ , by adding phenylmagnesium bromide to diethyl *o*-methoxybenzalmonate in 16% yield, and reported that the addition of *o*-methoxyphenylmagnesium bromide to benzalmonate failed.

(19) H. Bauer and P. Vogel, *J. prakt. Chem.*, [2] **88**, 329 (1913). We have found that the use of benzoic acid (5 g. per 5 ml. of piperidine) as a catalyst and the continuous removal of water by distillation of benzene improves the yield.

for 30 min. at 0–10° was left overnight at room temperature before work-up. Distillation afforded an oil, b.p. 223–225° at 3 mm., which solidified and gave IIc as a solid, m.p. 43.5–44.5°, in 91% yield. When this reaction was run without cuprous bromide the yield of IIc was 50%.

Addition of phenylmagnesium bromide to a benzene solution of diethyl benzalmonate containing cuprous bromide at –5–0° as above afforded diethyl benzhydrylmalonate,<sup>21</sup> b.p. 172–178° at 1 mm., m.p. 62–63°, in 93% yield.

*Anal.* Calcd. for  $C_{21}H_{24}O_5$ : C, 70.8; H, 6.7. Found: IIa<sup>m</sup>, C, 70.8; H, 7.0. IIb<sup>s</sup>, C, 70.6; H, 6.9. IIc<sup>m</sup>, C, 71.1; H, 6.8.

**2-Benzhydryl-1,3-propanediols (IIIa,b,c,d).**—Each of the above esters IIa,b,c,d was reduced by adding their benzene solutions slowly to stirred suspensions of excess lithium aluminum hydride in ether. The mixtures were then held at reflux for 2 hr. and treated with ethyl acetate to react with excess hydride. The reaction mixtures were then treated with dilute hydrochloric acid and the products isolated in the usual way. Compound IIIa was isolated as a colorless white finely crystalline solid, m.p. 72–73°, in 94% yield by low temperature crystallization from alcohol; IIb was distilled, b.p. 190–195° at 1 mm., to yield a viscous glass in 94% yield. A sample, b.p. 192° at 1 mm., was analyzed. Compound IIIc was obtained as shiny colorless needles, m.p. 61–62°, from benzene in 95% yield.

*Anal.* Calcd. for  $C_{17}H_{20}O_3$ : C, 75.0; H, 7.4. Found: IIIa<sup>m</sup>, C, 75.1; H, 7.5. IIIb<sup>s</sup>, C, 75.2; H, 7.5. IIIc<sup>m</sup>, C, 75.0; H, 7.5.

Compound IIId was obtained as a colorless glass, b.p. 182–185° at 2 mm., in 91% yield. After standing for 3 months, it crystallized and melted at 62–64°.

*Anal.* Calcd. for  $C_{16}H_{18}O_2$ : C, 79.3; H, 7.4. Found<sup>m</sup>: C, 79.0; H, 7.4.

**$\beta$ -Benzhydrylglutaronitriles (Va,b,c,d).**—In general, 40 ml. of methanesulfonyl chloride was added during 1 hr. to a stirred solution of 35 g. of IIIa in 200 ml. of dry pyridine at –10–0°. After stirring for 4 hr. more at –5° the mixture was poured on ice and dilute hydrochloric acid and the product was isolated in the usual way. In the cases of IVa,b,c the products were semisolids and were formed in about 95% yields. 2-Benzhydryl-1,3-propanediol bis-methanesulfonate (IVd) was isolated in 90% yield as colorless needles, m.p. 131–132° on crystallization from ethanol.

*Anal.* Calcd. for  $C_{18}H_{22}O_6S_2$ : C, 54.3; H, 5.5; S, 16.1. Found<sup>m</sup>: C, 54.3; H, 5.5; S, 15.7.

The above methanesulfonates (ca. 48 g.) were dissolved in 300 ml. of hot dimethylformamide and treated with solutions of potassium cyanide (30 g.) in 100 ml. of water. After heating at 90° with stirring for 4 hr., the cooled mixtures were poured on ice and products isolated in the usual way. After crystallization (using charcoal),  $\beta$ -o-methoxybenzhydrylglutaronitrile (Va) was obtained in 88% yield (over-all from IIIa) from benzene–cyclohexane as colorless crystals, m.p. 100–101°, after a preliminary crystallization from methanol.  $\beta$ -m-Methoxybenzhydrylglutaronitrile (Vb) was obtained in 86% yield (over-all from IIb) from methanol as colorless cubes, m.p. 91–92°, in 90% yield.  $\beta$ -p-Methoxybenzhydrylglutaronitrile (Vc) was obtained in 89% yield (over-all from IIIc) from benzene and Skellysolve B as colorless cubes, m.p. 132–133°, in 94% yield; and  $\beta$ -benzhydrylglutaronitrile (Vd) was obtained from benzene–Skellysolve B (petroleum ether, b.p. 65–70°) as colorless prisms, m.p. 135.0–135.5°, in 92% yield.

*Anal.* Calcd. for  $C_{19}H_{19}N_2O$ : C, 78.6; H, 6.2; N, 9.7. Found: Va<sup>m</sup>, C, 78.5; H, 6.1; N, 9.5. Vb<sup>s</sup>, C, 78.4; H, 6.3; N, 9.6. Vc<sup>m</sup>, C, 78.5; H, 6.4; N, 9.5. Calcd. for  $C_{18}H_{16}N_2$ : C, 83.1; H, 6.2; N, 10.8. Found: Vd<sup>m</sup>, C, 82.9; H, 6.0; N, 10.7.

**$\beta$ -Benzhydrylglutaric Acids (VIa,b,c,d).**—In a typical hydrolysis, 30.0 g. of Va, 50 g. of sodium hydroxide, and 500 ml. of ethylene glycol were heated with vigorous stirring at 180–190° for 3 hr. In the case of Vb and Vc the temperature was held at 175°. During this heating a heavy precipitate of the disodium salts appeared. When the evolution of ammonia had almost ceased the mixture was cooled and the precipitate collected. No good product was obtained from these filtrates. The precipitate was dissolved in boiling water and this solution filtered. The filtrate was added to excess hydrochloric acid and the acids recrystallized. There were obtained: VIa, m.p. 164.0–164.5°, in 89% yield from benzene–cyclohexane; VIb, m.p. 90.5–92.0°, in 82% yield from xylene; VIc, m.p. 129–130°, in 78% yield from xylene; and VId,<sup>14</sup> m.p. 176–177°, in 72% yield from benzene.

*Anal.* Calcd. for  $C_{19}H_{20}O_6$ : C, 69.5; H, 6.1. Found: VIa<sup>m</sup>, C, 69.4; H, 6.1. VIb<sup>s</sup>, C, 69.3; H, 6.1. VIc, C, 69.4; H, 6.0.

**Diketones VIIa,b,c.**—In a typical experiment 3.0 g. of VIa was stirred into 60 g. of polyphosphoric acid<sup>22</sup> held at 120  $\pm$  2°.

(20) C. A. Holmberg, *Chem. Abstr.*, **45**, 558c (1951), has prepared this compound but gives no melting point.

(21) E. P. Kohler, *Am. Chem. J.*, **34**, 134 (1905).

After 40 min. (30 min. for VIb at 125°, 40 min. for VIc at 125°) the color had changed from pale yellow to dark brown so the mixture was poured on 500 g. of ice. The solid was collected, washed with sodium carbonate solution (no starting acids were recovered by acidifying these extracts), dried, and recrystallized from benzene–isopropyl alcohol to yield 2.6 g. (98%) of 5,8-diketo-5,6,6a,7,8,12b-hexahydro-1-methoxybenzo[c]phenanthrene (VIIa), m.p. 175–178°. Similarly, 5,8-diketo-5,6,6a,7,8,12b-hexahydro-2-methoxybenzo[c]phenanthrene (VIIb), m.p. 141–142°, was obtained in 95% yield, and the 3-methoxy analog VIIc, m.p. 196–198°, in 90% yield from benzene–ethanol.

*Anal.* Calcd. for  $C_{19}H_{18}O_3$ : C, 78.1; H, 5.5. Found: VIIa<sup>m</sup>, C, 78.0; H, 5.6. VIIb<sup>s</sup>, C, 78.0; H, 5.5. VIIc<sup>m</sup>, C, 78.1; H, 5.7.

**Dialcohols VIIIa,b,c.**—In a typical experiment a solution of 1.5 g. of sodium borohydride and 0.2 g. of sodium hydroxide in 50 ml. of methanol were added during 30 min. to a suspension of 14.6 g. of VIIa in 200 ml. of methanol. After stirring for 2 hr. at room temperature and 2 hr. at 50°, the excess reagent was destroyed with acetone and the volume reduced to 50% under vacuum. The solution was diluted with water, acidified with hydrochloric acid, and further concentrated under vacuum. Isolation as usual yielded an oil which slowly crystallized. Two recrystallizations from benzene–Skellysolve B afforded 12.1 g. (82%) of a mixture of stereoisomers of 5,8-dihydroxy-5,6,6a,7,8,12b-hexahydro-1-methoxybenzo[c]phenanthrene (VIIIa), m.p. 85–90°, as a pale yellow powder. This, and less pure similar material, was suitable for further treatment. In the cases of the 2-methoxy isomer VIIIb and 3-methoxy isomer VIIc, higher yields were obtained as the entire reduced product (none of which had ketonic absorption in the infrared) was used in subsequent treatment. Compounds VIIIb, m.p. of pure sample 174–177°, from benzene and VIIc, m.p. 195–196°, from methanol were obtained in 94 and 96% yields (crude).

*Anal.* Calcd. for  $C_{19}H_{20}O_4$ : C, 77.0; H, 6.8. Found: VIIIa<sup>m</sup>, C, 76.8; H, 6.8. VIIIb<sup>s</sup>, C, 76.7; H, 6.8. VIIc<sup>m</sup>, C, 76.8; H, 6.9.

**Methoxybenzo[c]phenanthrenes (IXa,b,c).**—In the best of several procedures tried, a solution of 11.8 g. of VIIa in 100 ml. of xylene was heated to boiling in a flask equipped with a phase-separating head. On addition of 50 mg. of iodine, much dehydration occurred and the iodine color was discharged after a short time. Several other additions of small amounts of iodine were made during a 6-day period.<sup>23</sup> A total of 100 mg. of iodine was used. After each addition of iodine there was a longer period before the iodine color essentially disappeared, a signal to add more iodine. At the end, the color did not fade appreciably after 12 hr. at reflux. The xylene solution was then cooled, shaken with sodium bisulfite solution, and worked up as usual; the residue was treated with 1.28 g. of sulfur at 240–250° for 30 min., and then distilled over 1.5 g. of zinc dust at 1.5 mm. The yellow viscous distillate was chromatographed over Woelm grade 1 neutral alumina in benzene. The first fraction to be eluted was crystallized from benzene–ethanol and then from carbon disulfide at low temperature (–10°). There was obtained 7.9 g. (77%) of 1-methoxybenzo[c]phenanthrene, m.p. 137.0–138.0°, as thin colorless prisms.

*Anal.* Calcd. for  $C_{19}H_{14}O$ : C, 88.4; H, 5.4. Found<sup>m</sup>: C, 88.3; H, 5.4.

When VIIa (also VIIb and VIIc) were given only a treatment with iodine<sup>23</sup> the product consisted of a mixture of aromatic and dihydro derivatives. When freshly dehydrated materials from VIIa (etc.) were treated directly with sulfur much tar was formed. Dehydration and dehydrogenation over palladium-on-charcoal gave unsatisfactory results.

On treatment of IXa in benzene with slightly less than one equivalent of 2,4,7-trinitrofluorenone<sup>24</sup> (TNF), a black complex, m.p. 211–212.5°, separated. On concentration of the mother liquor and cooling, a brown-red complex, m.p. 156–157°, was obtained. Both complexes gave analytical results in agreement with a 1:1 complex, and pure IXa was recovered from each on chromatography over alumina.

*Anal.* Calcd. for  $C_{22}H_{19}N_3O_5$ : C, 67.0; H, 3.3; N, 7.3. Found<sup>s</sup>: C, 67.1; H, 3.1; N, 7.2 (for 212° isomer). C, 66.8; H, 3.3; N, 7.2 (for 157° isomer).

As in the case above, VIIb was converted into 2-methoxybenzo[c]phenanthrene (IXb) in 77% yield. The purest sample of IXb formed colorless leaflets, m.p. 76.5–77.0°, and an orange picrate, m.p. 119–120°, both in agreement with reported values.<sup>11</sup>

Similarly, VIIc was converted into 3-methoxybenzo[c]phenanthrene<sup>11b</sup> (IXc), m.p. 89–90°, in 71% yield. The orange picrate,<sup>11b</sup> m.p. 120.5–121.5°, was formed in methanol.

(22) We thank the Victor Chemical Co. for a generous gift of polyphosphoric acid.

(23) Compare M. S. Newman and D. K. Phillips, *J. Am. Chem. Soc.*, **81**, 3667 (1959).

(24) M. Orchin and O. Woolfolk, *ibid.*, **68**, 1727 (1946).

**Hydroxybenzo[c]phenanthrenes (Xa,b,c).**—In the best of several experiments a solution of 7.5 g. of IXa in 375 ml. of glacial acetic acid and 55 ml. of 48% hydrobromic acid was held at reflux until the first sign of turbidity was noted (260 min.). After cooling the acids were removed under reduced pressure and the residual brown oil was taken into 150 ml. of benzene. This solution was extracted with 10% sodium carbonate solution until almost colorless, and worked up as usual to yield a yellow oil which was chromatographed over silica gel using benzene. A small amount of deep yellow oil passed through first (later discarded) followed by 2.15 g. of starting IXa. The desired Xa then came through as a pale yellow oil which crystallized on trituration with Skellysolve B. After recrystallization from benzene and cyclohexane 3.1 g. (61% allowing for recovered IXa) of 1-hydroxybenzo[c]phenanthrene (Xa), m.p. 125–126° (OH band at 2.85  $\mu$ , 3500 cm.<sup>-1</sup>), was obtained.

The TNF derivative, red-brown needles, m.p. 166.5–167.0°, was formed in, and recrystallized from, benzene.

In the cases of IXb and IXc, demethylation was effected in almost quantitative yield as follows. A mixture of 3.0 g. of IXb, 120 ml. of acetic acid, and 70 ml. of 48% hydrobromic acid was held at reflux for 15 hr. After a work-up as for Xa, except that the chromatography was not needed, the crude product was crystallized from cyclohexane twice (using charcoal) to yield 2.6 g. (92%) of colorless 2-hydroxybenzo[c]phenanthrene,<sup>11a</sup> m.p. 114–115°; a sublimed sample absorbed at 3.1  $\mu$  (3220 cm.<sup>-1</sup>) and melted at 116.0–117.5°. This compound turns light pink on exposure to light and air, but the m.p. is not affected. The TNF derivative, m.p. 187–188° from benzene, was obtained as dark red-brown needles.

In a similar way, IXc yielded crude Xc in almost quantitative yield. Purification could be effected either by two crystallizations using charcoal, as above, or *via* the orange picrate, m.p. 149–150°, from methanol. The TNF derivative of Xc formed red-brown needles, m.p. 183–184° from benzene.

*Anal.* Calcd. for C<sub>24</sub>H<sub>15</sub>N<sub>3</sub>O<sub>8</sub>: C, 60.9; H, 3.2. Found<sup>m</sup>: C, 61.1; H, 3.3.

Decomposition of the picrate with ammonia afforded pure 3-hydroxybenzo[c]phenanthrene, m.p. 112.0–113.0° (OH band at 3.03  $\mu$ , 3300 cm.<sup>-1</sup>). This compound also turns pink on standing.

*Anal.* Calcd. for C<sub>18</sub>H<sub>12</sub>O: C, 88.5; H, 4.9. Found<sup>m</sup>: C, 88.4; H, 4.7 (for Xa). C, 88.4; H, 4.9 (for Xc). Calcd. for C<sub>21</sub>H<sub>17</sub>N<sub>3</sub>O<sub>8</sub>: C, 66.6; H, 3.0; N, 7.5. Found<sup>m</sup>: C, 66.6; H, 3.2; N, 7.4 (for Xa-TNF). C, 66.7; H, 3.2; N, 7.3 (for Xb-TNF). C, 66.6; H, 2.8; N, 7.1 (for Xc-TNF).

**5-Hydroxybenzo[c]phenanthrene (XIV).**— $\beta$ -Benzhydrylglutaric acid<sup>14</sup> (VID) was converted to 1-phenyl-1,2,3,4-tetrahydro-2-naphthylacetic acid as before<sup>14</sup> and the latter esterified to yield methyl 1-phenyl-1,2,3,4-tetrahydro-2-naphthylacetate, m.p. 95.5–96.0°.

*Anal.* Calcd. for C<sub>19</sub>H<sub>20</sub>O<sub>2</sub>: C, 81.4; H, 7.1. Found<sup>m</sup>: C, 81.4; H, 7.1.

A mixture of 5.0 g. of this ester and 1.14 g. of sulfur was heated at 250–255° for 40 min. Zinc dust was added and vacuum distillation afforded an ester which was not purified but hydrolyzed to the acid with alkali. The yield of pure 1-phenyl-2-naphthylacetic acid (XIII), m.p. 158–159°, was 64%.

*Anal.* Calcd. for C<sub>18</sub>H<sub>14</sub>O<sub>2</sub>: C, 82.5; H, 5.3. Found<sup>m</sup>: C, 82.6; H, 5.5.

A solution of 7.2 g. of XIII in 100 ml. of hydrogen fluoride was allowed to stand for several hours until the hydrogen fluoride had evaporated. After the usual work-up the crude product was chromatographed over silica gel using ether. Crystallization from benzene afforded 5.7 g. (85%) of colorless XIV, m.p. 133–134°, which turned pink or light tan on standing. The OH band is at 3.02  $\mu$  (3310 cm.<sup>-1</sup>). After standing for 10 months the sample had deteriorated markedly and a carbonyl peak at 5.90  $\mu$  was observed. This material (2.6 g.) was refluxed for 16 hr. with 5 g. of zinc dust (activated with Cu) and 250 ml. of 30% sodium hydroxide solution with stirring. After isolation as usual, 2.3 g. of pure XIV was recovered.

*Anal.* Calcd. for C<sub>18</sub>H<sub>12</sub>O: C, 88.5; H, 4.9. Found<sup>s</sup>: C, 88.3; H, 4.9.

The TNF derivative, prepared in benzene, formed brown needles, m.p. 165–166°.

*Anal.* Calcd. for C<sub>21</sub>H<sub>17</sub>N<sub>3</sub>O<sub>8</sub>: C, 66.6; H, 3.0; N, 7.5. Found<sup>s</sup>: C, 66.5; H, 2.8; N, 7.4.

**4-Hydroxybenzo[c]phenanthrene (XII).**— $\gamma$ -2-Naphthylbutyric acid was prepared essentially as described<sup>26</sup> except that the aromatization of methyl  $\gamma$ -2-tetralylbutyrate was accomplished on a larger scale (100 g. of ester) by heating slowly from 230 to 300° during 75 min. over 1 g. of 5% palladium-on-carbon catalyst (Engelhard Industries). The yield of  $\gamma$ -2-naphthylbutyric acid,<sup>26</sup>

m.p. 97–98°, was 97%. Cyclization to 4-keto-1,2,3,4-tetrahydrophenanthrene was accomplished in essentially quantitative yield by anhydrous hydrogen fluoride<sup>27</sup> (1 l. for 185 g. of acid). Methyl 1,2-dihydro-4-phenanthrylacetate, b.p. 188–189° at 1–2 mm., was prepared in 87% yield as described.<sup>13</sup> On heating 90 g. of this ester with 13 g. of sulfur at 240° for 45 min., a conventional work-up, which included refluxing for 1 hr. with aqueous alcoholic potassium hydroxide solution, afforded 58 g. (69%) of 4-phenanthrylacetic acid,<sup>27</sup> m.p. 173–174°. Methyl 4-phenanthrylacetate, b.p. 171–172° at 1 mm., was obtained as a viscous colorless oil in 86% yield.

*Anal.* Calcd. for C<sub>17</sub>H<sub>14</sub>O<sub>2</sub>: C, 81.6; H, 5.6. Found<sup>m</sup>: C, 81.6; H, 5.6.

Lithium aluminum hydride reduction of 50.0 g. of this ester (3 hr. at reflux in ether) and a conventional work-up yielded 37.5 g. (84%) of  $\beta$ -4-phenanthrylethanol as colorless cubic crystals, m.p. 75.8–76.6°, from benzene–cyclohexane (1:2).

*Anal.* Calcd. for C<sub>18</sub>H<sub>14</sub>O: C, 86.5; H, 6.3. Found<sup>m</sup>: C, 86.3; H, 6.3.

To a solution of 11.1 g. of this alcohol in 70 ml. of dry pyridine at –10 to –5° was added slowly 8 ml. of methanesulfonyl chloride. After 4 hr. at –5° the mixture was poured on ice and worked up as usual. On recrystallization from ethanol there was obtained 14.7 g. (98%) of  $\beta$ -4-phenanthrylethyl methanesulfonate, as colorless needles, m.p. 80.5–81.5°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>16</sub>O<sub>3</sub>S: C, 68.0; H, 5.3; S, 10.7. Found<sup>s</sup>: C, 67.8; H, 5.4; S, 10.6.

A hot solution of 14.5 g. of the above methanesulfonate in 300 ml. of absolute alcohol was added to a solution of the sodium derivative of diethyl malonate (16.2 g. of ester) in 150 ml. of alcohol. After being refluxed for 16 hr., much of the alcohol was removed under reduced pressure. The crude ester was isolated as usual and hydrolyzed with aqueous alcoholic potassium hydroxide. The malonic acid was isolated as usual to yield 14.0 g. (94%) of colorless needles, m.p. 156° dec., of  $\beta$ -(4-phenanthrylethyl)-malonic acid from benzene.

*Anal.* Calcd. for C<sub>19</sub>H<sub>16</sub>O<sub>4</sub>: C, 74.0; H, 5.2. Found<sup>m</sup>: C, 73.9; H, 5.4.

On decarboxylation by heating at 175° for 10 min., there was obtained colorless  $\gamma$ -4-phenanthrylbutyric acid,<sup>13</sup> m.p. 141–142°, in 77% yield. Cyclization of this in hydrogen fluoride afforded 4-keto-1,2,3,4-tetrahydrobenzo[c]phenanthrene<sup>13</sup> (XI), m.p. 126–127°, in 75% yield.

In a typical experiment 1.0 g. of XI in 20 ml. of *p*-cymene containing 0.5 g. of 5% palladium-on-carbon was heated at reflux under nitrogen for 2 hr. After filtration, removal of the solvent under vacuum, and crystallization from benzene–Skellysolve B and from cyclohexane, there was obtained 0.70 g. (71%) of 4-hydroxybenzo[c]phenanthrene (XII) as colorless leaflets, m.p. 110–111° (infrared 3.05  $\mu$ , 3300 cm.<sup>-1</sup>). The crystals turn to pale tan on standing.

*Anal.* Calcd. for C<sub>18</sub>H<sub>12</sub>O: C, 88.5; H, 4.9. Found<sup>s</sup>: C, 88.3; H, 4.8.

**6-Hydroxybenzo[c]phenanthrene (XIX).**—Methyl *o*-1-naphthylbenzoate (XV), m.p. 82–83° (lit.<sup>28b</sup> m.p. 87–88°; we probably had a polymorphic form as the corresponding acid had the correct m.p.), was reduced with lithium aluminum hydride to *o*-1-naphthylbenzyl alcohol (XVI), m.p. 89–90°, in 86% yield (crystallized from benzene–cyclohexane).

*Anal.* Calcd. for C<sub>17</sub>H<sub>14</sub>O: C, 87.2; H, 6.0. Found<sup>m</sup>: C, 87.0; H, 5.9.

The alcohol XVI (30 g.) was converted into the methanesulfonate as for  $\beta$ -4-phenanthrylethanol. The crude derivative was heated at 80–90° with a solution of 20 g. of potassium cyanide in 70 ml. of water, 0.1 g. of potassium iodide, and 200 ml. of dimethylformamide for 3 hr. The nitrile XVII was isolated as usual as an oil, b.p. 177–180° at 1–2 mm., in 53% yield. This solidified on standing to give XVII, m.p. 54.0–55.2°.

*Anal.* Calcd. for C<sub>18</sub>H<sub>13</sub>N: C, 88.9; H, 5.4; N, 5.8. Found<sup>s</sup>: C, 88.7; H, 5.4; N, 5.8.

A stirred mixture of 12.2 g. of XVII, 30 g. of potassium hydroxide, and 300 ml. of ethylene glycol was heated at 190° for 2 hr. A jelly formed on cooling and 100 ml. of water was added. The potassium salt of XVIII separated, was collected by filtration, and was washed with a little cold water. This salt was then recrystallized from 300 ml. of water. A hot aqueous solution of this salt was added to hydrochloric acid. The acid was recrystallized from benzene to yield 12.9 g. (98%) of colorless *o*-1-naphthylphenylacetic acid (XVIII), m.p. 62–65°. Further recrystallization did not improve the m.p.

(27) This method proved superior to those described: ref. 26b and M. S. Newman, *J. Am. Chem. Soc.*, **64**, 2131 (1942).

(28) (a) F. G. Badder and F. L. Warren, *J. Chem. Soc.*, 401 (1938); (b) W. M. S. Grieve and D. H. Hay, *ibid.*, 108 (1938).

(25) M. S. Newman and H. V. Zahm, *J. Am. Chem. Soc.*, **65**, 1097 (1943).

(26) (a) W. Borsche, *Ber.*, **52**, 2077 (1919); (b) R. D. Haworth, *J. Chem. Soc.*, 1125 (1932).

TABLE II  
 ULTRAVIOLET SPECTRA ( $m\mu$  (log  $\epsilon$ )) IN 95% ETHANOL

Benzo[c]-phenanthrene <sup>a</sup>	218 (4.70)	229 (4.36)	245 <sup>s</sup> (3.99)	254 <sup>s</sup> (4.16)	263.5 <sup>s</sup> (4.48)	271.5 (4.76)	281.5 (4.90)	294.5 <sup>s</sup> (4.09)	302 (4.03)	314.5 (4.00)	326.5 (3.63)	354.5 (2.52)	363 (2.29)	372 (2.30)
Xa	221 (4.43)			205 <sup>s</sup> (4.07)			281.5 (4.57)		306 (4.17)		326 <sup>s</sup> (3.85)	345 <sup>s</sup> (3.61)	364 (3.35)	383 (3.27)
Xb	219 (4.51)	232 (4.37)	246 <sup>s</sup> (4.22)	251.5 (4.23)		277 (4.58)	286.5 (4.55)		307 (4.19)	316 <sup>s</sup> (4.04)	330 <sup>s</sup> (3.65)	346 (3.32)	364 (3.44)	383 (3.46)
Xc	219 (4.59)			249 <sup>s</sup> (4.04)		278 <sup>s</sup> (4.64)	283.5 (4.72)		307.5 (3.92)	320.5 (3.95)	333 <sup>s</sup> (3.76)		363 (3.44)	380 (3.40)
XII	219.5 (4.59)		240.5 <sup>s</sup> (4.31)		268 (4.50)	280 (4.62)	291.5 (4.68)		303.5 (4.38)	322 <sup>s</sup> (4.06)		341 <sup>s</sup> (3.94)	362 <sup>s</sup> (3.69)	381 (3.62)
XIV	219 (4.57)	229 <sup>c</sup> (4.41)	242 <sup>c</sup> (4.15)	257 <sup>b</sup> (4.22)	268.5 <sup>s</sup> (4.48)	278.5 (4.72)	288.5 (4.81)		311 (4.10)	322 <sup>s</sup> (4.08)	337.5 (3.99)		365 (3.71)	382.5 (3.69)
XIX	219 (4.62)	236 (4.40)		253 (4.35)	268 <sup>s</sup> (4.52)	278.5 (4.69)	288.5 (4.62)		306.5 (4.35)	318.5 (4.24)		350 (3.65)	368.5 (3.76)	387 (3.79)
IXa	221 (4.57)			248 <sup>s</sup> (4.10)			281 (4.72)		303.5 (4.27)	321 <sup>s</sup> (3.95)	336 <sup>s</sup> (3.79)		361.5 (3.35)	381 (3.29)
IXb	218 (4.51)	232.5 (4.42)		251 (4.22)		277 (4.62)	286.5 (4.61)		305.5 (4.22)	316 <sup>s</sup> (4.08)		346 (3.48)	359 (3.56)	380.5 (3.57)
IXc	220 (4.40)			248 <sup>s</sup> (3.87)		277.5 <sup>s</sup> (4.46)	283 (4.60)		306 (3.79)	318 (3.80)	332 <sup>s</sup> (3.63)		360 (3.26)	378 (3.24)

<sup>a</sup> First three points were taken from E. Clar and D. G. Stewart, *J. Am. Chem. Soc.*, **74**, 6235 (1952); the rest of the figures for benzo[c]phenanthrene were taken from Shell Development Co., A.P.I. Research Project No. 44, 596 (1955) [*Org. Electronic Spectral Data*, **2**, 546 (1953-1955)].

 TABLE III  
 DATA FOR THE SPECTROPHOTOMETRIC DETERMINATION OF THE  $pK_a$  OF 1-HYDROXYBENZO[c]PHENANTHRENE (Xa)  
 Concentration 12.0 mg./l.; temp. 25°; 50% by weight ethanol

Wave length, $m\mu$	Absorbancy				$\log \frac{A_B - A_{NaOH}}{A_{HClO_4} - A_B}$		$pK_a$	
	In $HClO_4$ (f)	In $NaOH$ (g)	In pH 11.18 buffer (h)	In pH 11.78 buffer (i)	B (h)	B (i)	B (h)	B (i)
375	0.033	0.260	0.130	0.202	0.13	1.54	11.31	11.32
380	.039	.267	.135	.209	.14	1.53	11.32	11.31
385	.044	.251	.133	.200	.13	1.52	11.31	11.30
390	.020	.249	.117	.189	.13	1.55	11.31	11.33

Anal. Calcd. for  $C_{18}H_{14}O_2$ : C, 82.5; H, 5.3. Found<sup>a</sup>: C, 82.6; H, 5.5.

Cyclization of 12.0 g. of XVIII in 100 ml. of hydrogen fluoride yielded a reddish solid which was purified by chromatography in ether over silica gel to yield 8.0 g. (71%) of 6-hydroxybenzo[c]phenanthrene (XIX) as a light tan solid, m.p. 158.5-159.5°. We were unable to obtain colorless XIX. On standing, the color darkened. The purest sample was covered with nitrogen and kept in a well stoppered container out of the light. Even so, it turned darker in time although the m.p. was still about the same. In the infrared absorption there was a broad band at 2.95-3.08  $\mu$  (3400-3250  $cm^{-1}$ ).

Anal. Calcd. for  $C_{18}H_{12}O$ : C, 88.5; H, 4.9. Found<sup>a</sup>: C, 88.5; H, 5.0.

The TNF derivative formed red needles, m.p. 199-199.5°, from benzene.

Anal. Calcd. for  $C_{31}H_{17}N_3O_3$ : C, 66.6; H, 3.0; N, 7.5. Found<sup>a</sup>: C, 66.4; H, 3.1; N, 7.3.

The ultraviolet absorption spectra of the six hydroxybenzo[c]phenanthrols Xa,b,c, XII, XVI, and XIX as well as 1-methoxy-, 2-methoxy- and 3-methoxybenzo[c]phenanthrenes (IXa,b,c), were taken in 95% ethanol. The maxima are recorded in Table II. Shoulders are indicated by the superscript s. The similarity of the spectra of the hydroxy and methoxy compounds to that of parent hydrocarbon is readily seen.

**Ionization Constant Determinations.**—The method used previously for determination of the basicities of pyridines<sup>29</sup> was used. The  $pK_a$  of a phenol under test is given by the equation

$$pK_a = pH + \log \frac{A_B - A_{NaOH}}{A_{HClO_4} - A_B}$$

where pH is the value of a buffer solution and  $A_B$ ,  $A_{NaOH}$ ,  $A_{HClO_4}$  are the absorbancies of solutions of the phenol in the buffer, in 0.1 N sodium hydroxide solution, and 0.1 N perchloric acid solution, respectively, at a chosen wave length.

The following solutions were prepared in 50% aqueous ethanol: soln. a, 0.1 N sodium acetate; soln. b, 0.1 N perchloric acid;

soln. c, 0.1 N sodium hydroxide; soln. d, various buffers having pH values between 9.9 and 11.9, prepared by adding small quantities of soln. c to soln. a; soln. e, quantities of 5.0 to 11.0 mg. of the phenol (more or less in order to be able to observe the absorbancy in the sensitive regions of the apparatus) were weighed into 50-ml. volumetric flasks and filled up with soln. a; soln. f, 5 ml. of soln. e was diluted to 50 ml. with soln. b; soln. g, 5 ml. of soln. e was diluted to 50 ml. with soln. c. Solutions h and i were prepared by dilution of 5 ml. of soln. e to 50 ml. with a buffer (d). At least two such solutions were prepared for each phenol having pH values very close to the expected  $pK_a$ . Solutions a to d were used within 48 hr. and kept under nitrogen. Solutions e to i were freshly prepared before the measurements and were used within 1 hr.

The ultraviolet spectrum of each hydroxy compound in acidic and in basic media [soln. f and g] was determined and three to four suitable wave lengths were selected. After measuring the pH of the buffered solutions h and i (see below), the absorbancies of solutions f, g, h, and i were read on a Beckman spectrophotometer, Model DU. Each absorbancy was read at least twice (or as many times as necessary to get agreement) and determined against a reference having the same composition except for the phenol.

The pH of solutions h and i was determined immediately before and after the absorbancy readings, using a Beckman pH meter, Model N, a calomel reference electrode, and a glass electrode. Standardization of the apparatus was made by Beckman pH 7.00  $\pm$  0.02 buffer. During the pH measurements nitrogen was bubbled through the solutions in order to exclude carbon dioxide. When the pH of solution h or i decreased more than 0.02 pH unit the measurements were repeated using a different buffer. When buffers with pH values too far from the  $pK_a$  value were used, again repetition was necessary, as this could increase the error of the logarithmic factor.

In Table III data for a typical determination of the  $pK_a$  value for 1-hydroxybenzo[c]phenanthrene (Xa) are given. In Table I the average  $pK_a$  values of all the hydroxy compounds are listed. The measurements with the phenanthrols were made at  $24 \pm 1^\circ$ . Those of the benzo[c]phenanthrols at  $26 \pm 1^\circ$ . The results are accurate to  $\pm 0.03 pK_a$  unit.

(29) H. C. Brown and X. R. Mihm, *J. Am. Chem. Soc.*, **77**, 1723 (1955).