dienone–phenol rearrangement was carried out by treating 0.26 g. of the 2-bromodienone IV in 5 cc. of acetic anhydride with 0.09 g. of concentrated sulfuric acid and allowing the solution to stand at room temperature for five hours. The mixture was poured into water, swirled to hydrolyze most of the acetic anhydride and the product was extracted with ether. After saponification by refluxing with 5% methanolic potassium hydroxide for seventy-five minutes, the crude 1-methyl-2-bromoestradiol was acetylated by means of acetic anhydride and pyridine, and the diacetate was precipitated by dilution with 5% hydrochloric acid. After recrystallization from ethanol, the colorless crystals (0.13 g., 53%) melted at 185–191°, $[\alpha]^{25}\text{D}$ + 126°. The analytical sample crystallized as colorless rosets of shiny needles and had the following constants: m. p. 192.5–194°, $[\alpha]^{25}\text{D}$ + 128°, maximum at 273 m$\mu$, log $E$ = 2.67, minimum at 256.5 m$\mu$, log $E$ = 2.44 (Fig. 2).

*Anal.* Calcd. for $C_{23}H_{29}O_4Br$: C, 61.47; H, 6.51; Br, 17.78. Found: C, 61.66; H, 6.58; Br, 18.10.

**(b) By Bromination of 1-Methylestradiol (VI).**—When a solution of 55 mg. of 1-methylestradiol (VI)[2] in 1.4 cc. of glacial acetic acid was warmed with 63 mg. of pyridine hydrobromide perbromide for *ca.* thirty seconds, decolorization resulted with evolution of hydrogen bromide. After standing for a few minutes, the product was precipitated by the addition of water, filtered, and acetylated as in (a) to give 60 mg. (70% over-all yield) of the diacetate of m. p. 188–192°. Further recrystallization led to crystals melting at 193–194.5°, $[\alpha]^{25}\text{D}$ + 125°, which gave no depression in m. p. when mixed with a sample prepared according to (a). The ultraviolet absorption spectrum was also practically identical with that shown for the above sample (method a), maximum at 272.5 m$\mu$, log $E$ = 2.70, minimum at 257.5 m$\mu$, log $E$ = 2.54.

**1-Methyl-2-bromoestradiol (Va).**—Sixty milligrams of the diacetate Vb on saponification with methanolic potassium hydroxide gave 40 mg. of 1-methyl-2-bromoestradiol (Va) of m. p. 166–167.5°. Recrystallization from hexane or dilute ethanol raised the m. p. to 167.5–169°, $[\alpha]^{24}\text{D}$ + 189°, 185°, maximum at 288.5 m$\mu$, log $E$ = 3.42, minimum at 257 m$\mu$, log $E$ = 2.70 (Fig. 2). The same material was obtained from samples of the diacetate prepared according to (a) and (b) above.

*Anal.* Calcd. for $C_{19}H_{25}O_2Br$: C, 62.47; H, 6.90; Br, 21.88. Found: C, 62.81; H, 7.05; Br, 21.63.

The authors are greatly indebted to Jean Rogers and Helen Dudek for assistance in the experimental work.

## Summary

It has been shown that while the bromination of $\Delta^1$-androsten-17-ol-3-one 17-hexahydrobenzoate (I) proceeded rapidly with the formation of the corresponding $\Delta^1$-2-bromo-3-ketone II, the latter reacted only slowly with bromine to form $\Delta^1$-2,4-dibromoandrosten-17-ol-3-one 17-hexahydrobenzoate (III). The dibromo compound was dehydrobrominated with collidine yielding a 2-bromo-1,4-dienone IV, which underwent the dienone–phenol rearrangement to 1-methyl-2-bromoestradiol (V). The latter was also obtained on direct bromination of 1-methylestradiol (VI), thus establishing a link between the two series.

SUMMIT, NEW JERSEY RECEIVED NOVEMBER 24, 1947

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

# Optical Activity of the 4,5-Phenanthrene Type: 4-(1-Methylbenzo[c]phenanthryl)-acetic Acid and 1-Methylbenzo[c]phenanthrene[1]

BY MELVIN S. NEWMAN AND WILLIAM B. WHEATLEY[2]

The theoretical considerations leading to the prediction of optical activity in compounds of the 4,5-dimethylphenanthrene type have been presented.[3] The structural feature necessary for this type of optical isomerism (called optical activity of the 4,5-phenanthrene type) involves the substitution in the 4 and 5 positions of phenanthrene of groups large enough to prevent their existence in the same plane as that of the aromatic rings. The preparation and resolution of one compound of this type, 4,5,8-trimethyl-1-phenanthrylacetic acid, have been described.[3b,c] In order to obtain an additional example of compounds exhibiting this type of optical activity we undertook the synthesis and resolution of 4-(1-methylbenzo[c]phenanthryl)-acetic acid, I. This has been successfully accomplished and is herein reported. We have also synthesized 1-methylbenzo[c]phenanthrene, II, the last monomethyl derivative of the parent hydrocarbon which remained to be prepared.[4] This compound is to be tested for carcinogenic activity.

The optical activity in I is undoubtedly due to the fact that the methyl group is forced out of the plane of the aromatic rings.[3c] The hydrocarbon, II, should also be capable of resolution but no suitable resolving agent for hydrocarbons is known. We hope to prepare such a resolving agent in the future. We are also planning to synthesize compounds with larger interfering groups so that more accurate studies on the rates of racemization can be made.

The synthetic methods used are outlined in the chart.

The mixture of unsaturated esters resulting from the Reformatsky reaction of ketone III and ethyl $\alpha$-bromopropionate was dehydrogenated

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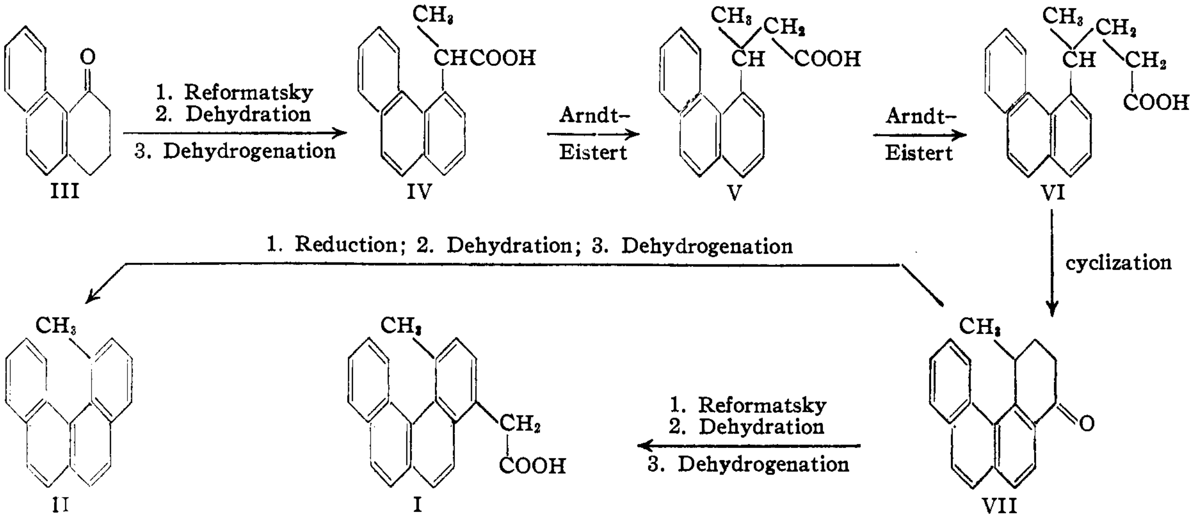
[1] The material herein presented was taken from the Ph.D. Thesis of W. B. W., The Ohio State University, June, 1947, and was presented before the Division of Organic Chemistry of the ACS, New York, September, 1947.

[2] Present address, Bristol Laboratories, Inc., Syracuse, New York.

[3] (a) Newman, THIS JOURNAL, **62**, 2295 (1940); (b) Newman and Hussey, *ibid.*, **69**, 978 (1947); (c) Newman and Hussey, **69**, 3023 (1947).

[4] 2-, 3- and 4-isomers, Hewett, *J. Chem. Soc.*, 1286 (1938); 5 isomer, Hewett, *ibid.*, 596 (1936); 6-isomer, Hewett, *ibid.*, 293 (1940).



over palladized charcoal to yield the acid, IV. As in the similar stage of the synthesis of 1,4,5-trimethylphenanthrene[3c] considerable cleavage to phenanthrene occurred during this step. The remaining steps occasioned no particular difficulty.

Two properties of the hydrocarbon, II, are of interest: its high melting point of 141.4–141.9° and its failure to yield a picrate. Since the melting point is higher than that of the parent benzo[c]phenanthrene or the other five monomethyl derivatives, which range from 54 to 81°, it was suspected that I might have been further cyclodehydrogenated into 1,12-methylenebenzo[c]phenanthrene, m. p. 134–135°, a compound previously synthesized from pyrene.[5] However, a comparison of physical and chemical properties indicated that our compound was decidedly different from that reported by Vollmann.[5] The failure to yield a picrate was surprizing in view of the fact that benzo[c]phenanthrene and the 2-, 3-, 4-, 5-, and 6-methylbenzo[c]phenanthrenes all give picrates. We were able to prepare a trinitrofluorenone[6] derivative.

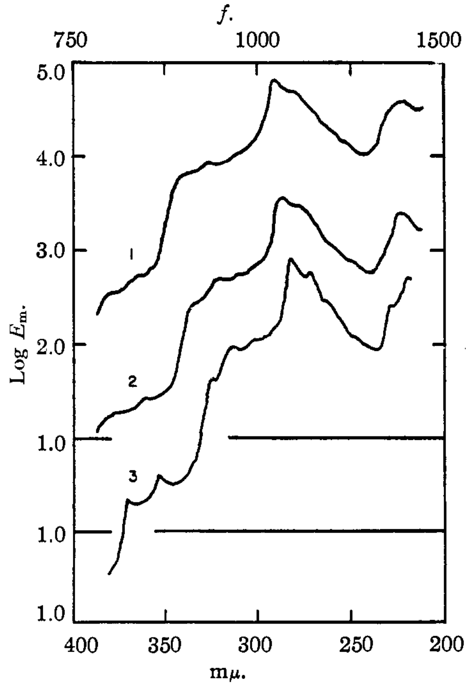


Fig. 1.—Ultraviolet absorption spectra: 1, 4-(1-methylbenzo[c]phenanthryl)-acetic acid; 2, 1-methylbenzo[c]phenanthrene; 3, benzo[c]phenanthrene. Curves 2 and 3 are dropped one and two log $E_m$ units, respectively, to avoid undue overlapping with Curve 1.

The ultraviolet absorption spectra of I and II are given in Fig. 1 where they are compared to that of benzo[c]phenanthrene.[7] It is easily seen that they resemble the parent hydrocarbon but that there is some loss of fine structure.

The resolution of the acid I was not accomplished without much trouble. We were not able to find a suitable salt of I with an alkaloid. By treating the acid chloride of I with *l*-menthol we were able to obtain a quantity of *d*-acid which had evidently not been esterified.[8] On recrystallization this acid gave specific rotations which varied from +1.0 to +2.1°. On standing the rotation gradually disappeared. In this respect, this acid behaved quite the same as that previously reported, 4,5,8-trimethyl-1-phenanthrylacetic acid.[3c]

We would like to take this opportunity to acknowledge a grant-in-aid from a special fund donated by the Ohio State University Research Foundation and administered by the Graduate School.

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(5) Vollman, *et al.*, *Ann.*, **531**, 135 (1937).

(6) Orchin and Woolfolk, THIS JOURNAL, **68**, 1727 (1946).

(7) The curve for benzo[c]phenanthrene is reproduced from an article by Mayneord and Roe, *Proc. Roy. Soc. London*, **A152**, 299 (1935). The curve for benzo[c]phenanthrene as given by Clar in "Aromatische Kohlerwasserstoffe," Springer Verlag, 1941, p. 112, is incorrect. The curve is apparently that of 1',2'-naphtha-2,3-fluorene which is also given by Mayneord and Roe.

(8) Compare partial esterifications of Marckwald and McKenzie, *Ber.*, **32**, 2130 (1899).

## Experimental[9]

**α-4-Phenanthrylpropionic Acid, IV.**—A solution of 70 g. (0.357 mole) of ketone III[10] and 75 g. (0.415 mole) of ethyl α-bromopropionate in 400 cc. of dry benzene was added dropwise with stirring to 27 g. (0.415 mole) of hydrochloric acid-washed granular zinc. The reaction started easily upon the addition of a few crystals of iodine, and portions of iodine were added three times during the course of the reaction. Refluxing was maintained by external heating during the addition of the ketone–ester solution, which required about an hour, and for an additional two hours. After cooling, the reaction mixture was hydrolyzed with ice and hydrochloric acid and the organic matter taken into benzene and washed with saturated sodium bicarbonate solution. On removal of the last of the benzene, spontaneous dehydration of the crude hydroxyester occurred. Distillation *in vacuo* yielded 86 g. of an orange-red oil, which was saponified by refluxing one hour with dilute methanolic potassium hydroxide and the resulting mixture worked up into neutral and acidic fractions. The neutral fraction yielded 22.4 g. (32%) of recovered ketone, III; the acidic fraction was esterified in the usual manner with methanol and dry hydrogen chloride. Distillation gave 55.7 g. (59%, or 86% based on ketone consumed) of ester, a yellow oil boiling at 163–165 (1 mm.). The ester crystallized in part and on crystallization from low boiling petroleum ether, colorless stout needles, m. p. 67–72°, were obtained.

*Anal.* (d) Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 80.7; H, 6.9.

The acid obtained from this ester was crystallized from benzene until it melted at 176.6–177.2° dec.

*Anal.* (c) Calcd. for $C_{17}H_{16}O_2$: C, 80.9; H, 6.4. Found: C, 81.0, 81.1; H, 6.0, 6.2.

In the best of many experiments 160 g. (0.6 mole) of the above crude ester in four equal batches was dehydrogenated by heating with 20% palladium-on-charcoal catalyst for forty-five minutes at 280–320°; 40% of the theoretical quantity of hydrogen was collected during this time. The reaction product was worked up into neutral and acidic fractions. The neutral fraction, which amounted to 11.3 g., (10.5%) was identified as phenanthrene. Recrystallization of the crude acid from benzene gave 63.9 g. (43%) of acid melting above 215.8° and almost as much non-crystalline acid. By esterifying and further dehydrogenation more crystalline acid could be obtained from these non-crystalline fractions. A sample of acid recrystallized several times melted at 218.1–218.6°. *Anal.* (c) Calcd. for $C_{17}H_{14}O_2$: C, 81.6; H, 5.6. Found: C, 81.1; H, 5.8. Longer heating of the dihydroester with the catalyst caused more hydrogen to be evolved, but lower yields of crystalline acid were obtained, along with greater amounts of neutral material. Dehydrogenation with sulfur gave similar but inferior results.

**β-4-Phenanthrylbutyric Acid, V.**—A solution of 52.5 g. (0.21 mole) of acid IV, 30 cc. of purified thionyl chloride and 5 drops of pyridine in 750 cc. of dry ether was stirred for three hours at room temperature. Removal of solvent and excess thionyl chloride under reduced pressure left a solid residue which on recrystallization from benzene gave 41.1 g. (73%) of acid chloride. A solution of 32.5 g. (0.12 mole) of the above acid chloride in 400 cc. of dry ether was added dropwise over a period of three hours to a dry ethereal solution of diazomethane, prepared from 63 g. of N-nitrosomethylurea,[11] stirred vigorously and maintained at below 5° by an ice-bath.

After stirring overnight, during which time the solution came to room temperature, the ether was removed under reduced pressure. The solid yellow residue was suspended in 250 cc. of methanol and 75 cc. of dioxane and the suspension heated to 55°. Portions of freshly prepared silver oxide were added at ten-minute intervals to this diazoketone suspension and, after two hours of heating at 55°, the theoretical amount of nitrogen had been collected. After refluxing for an hour, the reaction mixture was filtered; the filtrate stripped and distilled *in vacuo*, yielding 27.3 g. of reddish oil which was saponified and worked up into neutral and acidic fractions. The neutral fraction, a dark red viscous oil, was discarded. The acidic fraction was recrystallized from benzene to give 16.3 g. (51%) of acid V, m. p. 143–145°. An analytical sample crystallized in colorless prisms, m. p. 145.8–146.5°.

*Anal.* (a) Calcd. for $C_{18}H_{16}O_2$: C, 81.8; H, 6.1; neut. equiv., 264. Found: C, 82.1, 81.9; H, 6.4, 6.5; neut. equiv., 263, 266.

**γ-4-Phenanthrylvaleric Acid, VI.**—An Arndt–Eistert synthesis was carried out on acid V in a manner similar to that described above. In this case, the rearrangement of the diazoketone proceeded more rapidly so that the theoretical amount of nitrogen was evolved in forty-five minutes. There was obtained by crystallization of the acid fraction from benzene a first crop of crystalline acid VI, m. p. 136.0–137.8° (57%) and a second crop melting at 135.6–137.2° (6%). An analytical sample melted at 138.4–139.0°.

*Anal.* (a) Calcd. for $C_{19}H_{18}O_2$: C, 82.0; H, 6.5; neut. equiv., 278. Found: C, 82.5, 82.1; H, 6.8, 6.4; neut. equiv., 280, 278.

**4-Keto-1-methyl-1,2,3,4-tetrahydrobenzo[c]phenanthrene, VII.**—To a well-stirred, ice-cold solution of the acid chloride of VI, prepared from 9.0 g. (0.00524 mole) of acid VI by treatment with thionyl chloride and pyridine as described above, in 100 cc. of anhydrous *sym*-tetrachloroethane was added rapidly 10 cc. of fuming stannic chloride. A yellow complex separated almost immediately. After thirty minutes the mixture was hydrolyzed with dilute hydrochloric acid and the solvent removed by steam distillation.

After vacuum distillation there was obtained 7.9 g. (95%) of ketone VII as a viscous yellow oil which solidified on standing a few weeks. An analytical sample, recrystallized from Skellysolve B, melted at 80.2–81.2°.

*Anal.* (b) Calcd. for $C_{19}H_{16}O$: C, 87.7; H, 6.2. Found: C, 87.6, 87.9; H, 6.3, 6.4.

The 2,4-dinitrophenylhydrazone of VII melted at 300–302° uncor. dec.

*Anal.* (b) Calcd. for $C_{25}H_{20}O_4N_4$: C, 68.2; H, 4.6; N, 12.7. Found: C, 68.2, 68.1; H, 4.6, 4.7; N, 12.5, 12.6.

**1-Methylbenzo[c]phenanthrene, I.**—After aluminum isopropoxide–isopropyl alcohol reduction of 4.87 g. (0.019 mole) of VII, dehydration of the resulting carbinol by heating to 215°, and vacuum distillation there was obtained 4.22 g. (92%) of a light yellow oil. A mixture of 4.10 g. (0.017 mole) of this oil and 0.525 g. (0.016 mole) of sulfur was heated for one hour at 205–225°, then immediately vacuum distilled, yielding 3.39 g. of light green oil. This oil was dissolved in petroleum ether b. p. 35–40° (Skellysolve F) and absorbed on a column of $-80$ mesh alumina. Elution with petroleum ether, b. p. 95–100° (Skellysolve C), followed by several recrystallizations of the crystalline material so obtained, gave 0.81 g. (20%) of colorless 1-methylbenzo[c]phenanthrene (I), m. p. 141.4–141.9°.

*Anal.* (b) Calcd. for $C_{19}H_{14}$: C, 94.2; H, 5.8. Found: C, 94.2, 94.2; H, 6.0, 6.1.

In contrast to the yellow hydrocarbon, m. p. 134–135° of Vollman,[5] I is colorless and gives a violet color in concentrated sulfuric acid rather than a yellow color with green fluorescence.[5] Furthermore, on chromic acid oxidation, no trace of the quinone mentioned by Vollman was obtained.

While several attempts to prepare the picrate I were unsuccessful, a derivative with 2,4,7-trinitrofluorenone was obtained in the following manner; equivalent amounts of

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[9] Analyses marked (a) by Arlington Laboratories, (b) by W. J. Polglase, (c) by S. Olsen, and (d) by D. Mowry. All melting points corrected unless otherwise noted.

[10] Bachmann and Edgerton, THIS JOURNAL, **62**, 2970 (1940).

[11] Adams, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1942, Vol. I, p. 50.

the hydrocarbon and trinitrofluorenone were dissolved in hot benzene. On standing in an ice box overnight, the solution deposited light yellow crystals, apparently the hydrocarbon. After several weeks in the ice box, a number of bright red clusters were present. These were picked out, washed in turn with benzene, acetone, and Skellysolve C, then dried *in vacuo;* m. p. 130.6–131.4°.

*Anal.* (b) Calcd. for $C_{32}H_{19}O_7N_3$: C, 68.9; H, 3.4; N, 7.5. Found: C, 68.7, 68.7; H, 3.5, 3.6; N, 7.6, 7.6.

**4-(1-Methylbenzo[c]phenanthryl)-acetic acid, II.**—To a solution of 11.12 g. (0.043 mole) of ketone VII in 150 cc. of dry benzene was added 6.0 g. (0.036 mole) of ethyl bromoacetate, 2.4 g. (0.036 mole) of granular zinc and a pinch of iodine. After fifteen minutes of refluxing, the reaction began. Five more like quantities of ester, zinc and iodine were added at half-hour intervals, during which time refluxing was maintained by external heating. Following hydrolysis with dilute hydrochloric acid, the benzene layer was separated and the aqueous layer washed twice with benzene. The combined benzene extracts were evaporated, the residual oil heated ten minutes at 190–200° to effect dehydration, and then distilled *in vacuo*. The distillate was saponified and the resulting product worked up to give a neutral fraction of 1.60 g. (14%) of recovered ketone and an acid fraction which was esterified with methanol–hydrogen chloride, yielding 8.57 g. (63%) of distilled ester.

A mixture of 7.08 g. (0.022 mole) of the above ester and 0.71 g. (0.022 mole) of sulfur was heated for one and one-half hours at 220°, then distilled *in vacuo*. The distillate was saponified, the acid fraction dissolved in acetone and passed through a column of charcoal (Norite A). There was obtained 3.86 g. (57%) of acid II melting above 208°. An analytical sample, colorless prisms from benzene–acetone, melted at 210.1–210.6°.

*Anal.* (b) Calcd. for $C_{21}H_{16}O_2$: C, 84.0; H, 5.4; neut. equiv., 300. Found: C, 83.7, 83.8; H, 5.3, 5.5; neut. equiv., 297, 300.

The amide of II, recrystallized from benzene–acetone, melted at 234.5–235.5° uncor.

*Anal.* (b) Calcd. for $C_{21}H_{17}ON$: C, 84.3; H, 5.7; N, 4.7. Found: C, 84.4, 84.4; H, 6.1, 5.9; N, 4.7, 4.7.

**Resolution of II.**—A solution of the chloride of acid II, prepared by treatment of 1.54 g. (0.0041 mole) of II with thionyl chloride and pyridine, in 50 cc. of dry benzene was added dropwise to a well-stirred ice-cold solution of 0.80 g. (0.0051 mole) of *l*-menthol ($[\alpha]_D$ −49.8°, *c*, 2 in absolute ethanol) in 25 cc. of dry benzene. After being stirred for an hour, during which time it came to room temperature, the reaction mixture was hydrolyzed. The benzene layer was separated, washed in turn with dilute hydrochloric acid, water, saturated sodium bicarbonate solution and then dried. Evaporation of the benzene under reduced pressure left an orange oil, which gave 0.39 g. of crystalline material on trituration with Skellysolve F. This material, after five recrystallizations from chloroform–Skellysolve F, melted at 185.5–187.0° and showed a specific rotation of +1.4 ± 0.2° (*c*, 1 in chloroform). Although it was at first believed that this material was the *l*-menthyl ester of II, the analysis indicated that it was impure.

*Anal.* (b) Calcd. for $C_{31}H_{34}O_2$ (ester): C, 84.9; H, 7.8. Calcd. for $C_{21}H_{16}O_2$ (acid): C, 84.0; H, 5.4. Found: C, 84.9, 84.9; H, 5.4, 5.4.

The five-times recrystallized material was shaken with alcoholic potassium hydroxide for ten minutes, the mixture then diluted with a large quantity of water and extracted repeatedly with ether. Acidification of the aqueous layer precipitated the acid, which was extracted with ether. Evaporation of the ether from the combined extracts left light tan crystals of acid II, m. p. 208.8–209.6°, alone and when mixed with an authentic sample of II. A solution of 0.1053 g. of this acid in 5 cc. of acetone gave an observed rotation of +0.09 ± 0.02°; $[\alpha]^{25}_D$ +2.1 ± 0.4°. No rotation could be observed the following day. Two other resolutions were carried out in the manner described above, giving samples of acid with specific rotations of +1.6 and +1.0°. The acetone solutions of both of these samples displayed no optical activity after standing for twelve hours at room temperature.

## Summary

The synthesis of 1-methylbenzo[c]phenanthrene is described. This synthesis completes the series of methylbenzo[c]phenanthrenes, as the other five isomers have been previously described.

The synthesis of 4-(1-methylbenzo[c]phenanthryl)-acetic acid is described, and the dextrorotatory form of this acid has been isolated. The isolation of this optically active acid provides another instance of optical activity of the 4,5-phenanthrene type.

Columbus 10, Ohio Received February 12, 1948

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[Contribution from the Central Research Laboratories, Monsanto Chemical Company]

# Vinyl Aromatic Compounds. V. Ortho-, Meta- and Para-Isopropenylbiphenyls[1]

By David T. Mowry, Joachim Dazzi, Mary Renoll[2] and Robert W. Shortridge[3]

In a preceding paper[4] the synthesis of ortho-, meta- and para-vinylbiphenyls from the corresponding xenylmethylcarbinols has been described. The present work deals with the preparation of the corresponding isopropenyl derivatives of biphenyl.

In general, the methods employed resembled those used in the earlier work. *o*-Aminobiphenyl was converted to *o*-iodobiphenyl, which by means of its Grignard reagent with acetone gave dimethyl-*o*-xenylcarbinol. This was dehydrated catalytically in the vapor phase over alumina to give *o*-isopropenylbiphenyl in 83% yield. It is interesting to note that under these conditions the reaction takes a different course from that reported by Anchel and Blatt[5] who dehydrated the same carbinol in the liquid phase with sulfuric acid or a mixture of acetic acid and hydrogen chloride to give nearly quantitative yields of 9,9-

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[1] Preceding paper in this series, This Journal, **69**, 851 (1947).

[2] Present address: Department of Chemistry, The Ohio State University, Columbus, Ohio.

[3] Present address: Midwest Research Institute, Kansas City, Missouri.

[4] Huber, Renoll, Rossow and Mowry, This Journal, **68**, 1109 (1946).

[5] Anchel and Blatt, *ibid.*, **63**, 1948–1952 (1941).