[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY]

Chemistry of Lactones. V. Reaction of α-Benzylidene-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide with Phenylmagnesium Bromide and Phenyllithium

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Received November 7, 1960

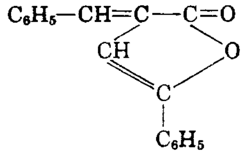
α-Benzylidene-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide (I) reacted with phenylmagnesium bromide to give the 1,4-addition products, α-benzhydryl-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide (II) and its $\Delta^{\alpha,\beta}$-tautomer (III). The relative amounts of these isomers could be varied because of the ready tautomerization of II to III. The structure of II was confirmed by its reactions with alkali and hydrogen. In contrast to the behavior with the Grignard reagent, the reaction of I with phenyllithium gave the ring opened product, 1,1-diphenyl-2-phenacylcinnamyl alcohol (IV), which readily cyclized to 2,2,5-triphenyl-3-benzylidene-2,3-dihydrofuran (XII).

In a previous paper[1] our studies on the ring opening reactions of α-benzylidene-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide (I) with some common strong nucleophiles were reported. Besides the β,γ-unsaturated-γ-lactone structure, I possesses the added feature of an α,β-unsaturated carbonyl system due to the benzylidene group exocyclic to the lactone ring. In a continuation of our research on highly conjugated lactone systems, the reactions of I with phenylmagnesium bromide and phenyllithium are described.

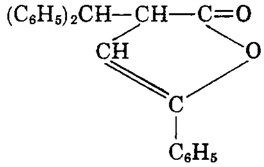
The lactone, I, reacted with excess phenylmagnesium bromide by 1,4-addition to the α,β-unsaturated carbonyl moiety to give as the main products a mixture of α-benzhydryl-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide (II) and its tautomer, α-benzhydryl-γ-phenyl-$\Delta^{\alpha,\beta}$-butenolide (III), the lactone ring remaining intact. In addition to II and III, a residue was obtained from which no pure substance could be isolated. The infrared spectrum of this material indicated the presence of both a carbonyl and a hydroxyl group, which might be attributed to the ring opened product (IV). Attempted formation of a 2,4-dinitrophenylhydrazone failed as did attempted ring closure with acetic anhydride.

The formation of II and III is in marked contrast with the results obtained by the reaction of this Grignard reagent with the structurally related 2-phenyl-4-benzylidene-5(4H)oxazolone (V), which is isoelectronic with I. It has been shown[2] that V reacts with phenylmagnesium bromide to give the ring opened 1,1-diphenyl-2-benzamidocinnamyl alcohol (VI) and the oxazoline (VII).

The structural assignments for II and III were confirmed by elemental analyses, spectral data, and by chemical evidence to be presented later.



I



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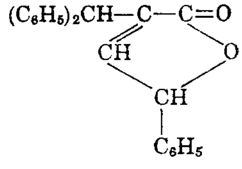
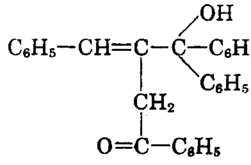
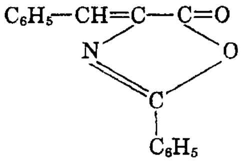


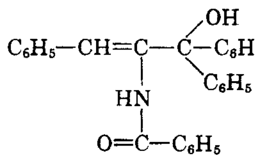
III



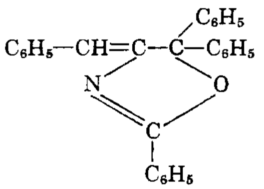
IV



V



VI



VII

Tautomer II exihibits an intense band at 1783 cm.$^{-1}$, characteristic of the carbonyl stretching frequency in β,γ-unsaturated-γ-lactones,[3] whereas the strong absorption of III at 1750 cm.$^{-1}$ is typical of α,β-unsaturated-γ-lactones. II possesses a maximum at 262 mμ which is probably due to the styrene chromophore while III shows only end absorption. These results are consistent with the structures proposed and correspond very closely to those observed by Ramirez and Rubin[4] with the α-methyl analogs of II and III.

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(1) R. Filler and L. M. Hebron, *J. Am. Chem. Soc.*, **81**, 391 (1959).

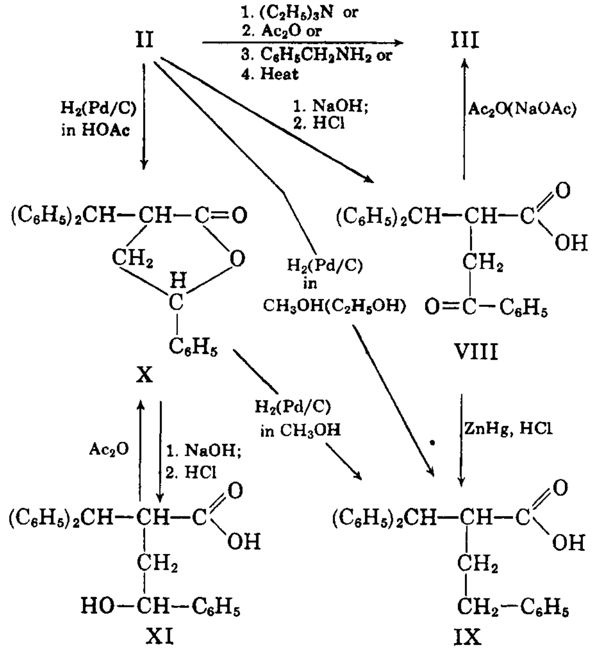
(2)(a) R. Filler and J. D. Wismar, *J. Org. Chem.*, **22**, 853 (1957); (b) H. Pourrat, *Bull. soc. chim. France*, 828 (1955); (c) A. Mustafa and A. H. E. Harhash, *J. Org. Chem.*, **21**, 575 (1956); (d) W. I. Awad and M. S. Hafez, *J. Org. Chem.*, **25**, 1180, 1183 (1960).

(3) J. F. Grove and H. A. Willis, *J. Chem. Soc.*, 877 (1951).

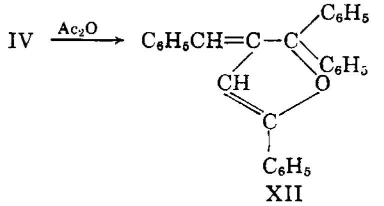
Compound II was converted to its tautomer (III) by acetic anhydride, triethylamine or benzylamine.[5] The tautomerization was also effected by heating II in the solid state. The course of this change was followed spectrophotometrically by the appearance and increase in intensity of the carbonyl absorption band at 1750 cm.$^{-1}$. Similarly, this conversion occurred in the isolation of the product from the reaction mixture when the ether solution was evaporated to dryness on a steam bath. Yields of 3% and 20% of II and III respectively, were obtained. This differs from the yields of 42% and 4% of II and III respectively, obtained when the solvent was evaporated at room temperature. Thus, II is the product of kinetic control and III the thermodynamically more stable isomer. The tautomerization may be attributed to the increased stability imparted by the conjugation of the butenolide double bond with the carbonyl group in III. Ramirez[4] has similarly observed that with the α-methyl analogs that the α,β-unsaturated compound is more stable than the β,γ-tautomer and is readily formed from it. Similar observations have been made regarding the relative stability of other α,β-unsaturated butenolides.[6-8]

An attempt to synthesize II by an alternate method failed,[9] but the reactions of II, summarized in the following chart, offer decisive chemical evidence for the structure proposed. In contrast, III did not undergo these reactions, probably due in large measure to its insolubility in most organic solvents.

Alkaline hydrolysis of II gave 2-phenacyl-3,3-diphenylpropionic acid (VIII) in 84% yield. Ring closure of VIII to III was effected by sodium acetate in acetic anhydride, presumably through II, whith tautomerized to III in this medium. The course of reaction of II with hydrogen using a palladium on charcoal catalyst was found to depend on the solvent employed. In ethanol or methanol, hydrogenation and hydrogenolysis occurred to give the saturated acid (IX) in 41% yield. The structure of IX was confirmed by its preparation from VIII by Clemmensen reduction. In acetic acid, only hydrogenation of II occurred to give the substituted butyrolactone (X) in 45% yield. The structure of X is supported by analytical and spectral data and by its alkaline hydrolysis to the γ-hydroxy acid (XI), which is reconverted to X on treatment with acetic anhydride. In methanol, X reacted with hydrogen to yield IX. Thus, it seems probable that II is hydrogenated to give the intermediate butyrolactone (X) which then undergoes hydrogenolysis to IX.



The reaction of I with phenyllithium did not follow the course observed with phenylmagnesium bromide. Instead, the sole product, isolated in 49% yield, was the ring opened compound, 1,1-diphenyl-2-phenacylcinnamyl alcohol (IV). Compound IV is highly unstable and develops a yellow-green color on standing, as well as by heating. This lability may be attributed to the facile ring closure of IV to form the yellow-green substituted dihydrofuran (XII). The latter was readily obtained while attempting to prepare the 2,4-dinitrophenylhydrazone, oxime or semicarbazone of IV, as well as by heating with acetic anhydride.



XII

EXPERIMENTAL[10]

α-Benzylidene-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide (I). This compound was prepared by the method of Schueler and Hanna.[11]

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[4] F. Ramirez and M. B. Rubin, *J. Am. Chem. Soc.*, **77**, 3768 (1955).

[5] The tautomerization of II by benzylamine is highly unusual, for the ring opening of lactones by this reagent is usually so facile that it is frequently used in determining the lactone content in mixtures (*The Chemistry of Penicillin*, H. T. Clarke, J. R. Johnson and R. Robinson, editors, Princeton University Press, Princeton, N. J., 1949, p. 735).

[6] W. Cocker and S. Hornsby, *J. Chem. Soc.*, 1157 (1947).

[7] M. S. Newman and C. O. Van der Werf, *J. Am. Chem. Soc.*, **67**, 233 (1945).

[8] F. Ramirez and M. B. Rubin, *J. Am. Chem. Soc.*, **77**, 2905 (1955).

[9] Unsuccessful efforts were made to prove the structure of II by reaction of α-phenacylcinnamic acid with benzene under Friedel-Crafts conditions (aluminum chloride). The expected 1,4-addition product could then have been ring closed with acetic anhydride to give II (and III). The failure of benzene to add to an α-substituted conjugated system has been observed with substituted acrylic acids (J. F. J. Dippy and J. T. Young, *J. Chem. Soc.*, 3919 (1955).

[10] All melting points are corrected.

Reaction of I *with phenylmagnesium bromide.* To 3.65 g. (0.15 g.-atom) of magnesium ribbon in 130 ml. of anhydrous ether was added dropwise 15.7 ml. (0.15 mole) of bromobenzene. After the reaction had subsided, the mixture was heated under reflux for 0.5 hr. and 12.4 g. (0.05 mole) of I, suspended in 500 ml. of ether, was added in portions over a 2-hr. period. The mixture was heated under reflux for an additional 2 hr. and then decomposed with an 8% solution of sulfuric acid. The ether layer was washed with water and dried over anhydrous magnesium sulfate. Evaporation of the ether solution by air blowing yielded a yellow solid. The crude product was crystallized from ethanol to give 6.8 g. (42%) of α-benzhydryl-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide (II), m.p. 156–158°. $\lambda_{max}^{C_2H_5OH}$ 262 mμ (ε 8500). Infrared absorption at 1783 cm.$^{-1}$ (s).

Anal. Calcd. for $C_{23}H_{18}O_2$: C, 84.64; H, 5.56. Found: C, 84.73; H, 5.77.

Air evaporation of the ether filtrate recovered from II gave an oily residue. The residue was dissolved in a minimum amount of dioxane and placed in a refrigerator for several days. A white solid separated and was crystallized from 300 ml. of dioxane to yield 0.64 g. (4%) of α-benzhydryl-γ-phenyl-$\Delta^{\alpha,\beta}$-butenolide (III), m.p. 281–282°.

Anal. Calcd. for $C_{23}H_{18}O_2$: C, 84.64; H, 5.56. Found: C, 84.60; H, 5.38.

$\lambda_{max}^{C_2H_5OH}$ End absorption. Infrared absorption at 1750 cm.$^{-1}$ (s).

When the ether solution was evaporated to dryness on a steam bath, rather than by air evaporation, an oil containing a suspended solid was obtained. This mixture was treated with a large quantity of petroleum ether (b.p. 60–80°).

Evaporation of the solvent gave 0.48 g. (3%) of II and an oily residue which was worked up in dioxane as described previously to yield 3.2 g. (20%) of III.

Evaporation of the dioxane filtrate from III gave a residue which had infrared absorption bands at 1750 cm.$^{-1}$, 1680 cm.$^{-1}$, and 3350 cm.$^{-1}$ The residue was treated with acetic anhydride and heated on a steam bath overnight. Only a small amount of III was obtained (less than 0.5%). Attempts to prepare a 2,4-dinitrophenylhydrazone of the residue were unsuccessful.

Tautomerization of II. II (0.8 g., 0.002 mole), dissolved in 37 ml. of benzene, was heated under reflux with 15 ml. (0.11 mole) of triethylamine for 18 hr. and 0.3 g. (38%) of a white solid was obtained, m.p. 279–282°. There was no melting point depression on admixture of this solid with an authentic sample of III.

Compound II was heated under reflux with a 10% solution of benzylamine in benzene for 2 hr. to give a 33% yield of III.

II (1.0 g., 0.0025 mole) dissolved in 25 ml. of acetic anhydride, was heated on a steam bath for 12 hr. to give 0.5 g. (50%) of III, m.p. 280–282°.

II (500 mg.) was heated for 3 hr. in an oven at 100°. The solid had a m.p. of 137–152°, infrared absorption (chloroform), 1783 cm.$^{-1}$ ($\Delta^{\beta,\gamma}$-butenolide). Further heating overnight yielded a solid, m.p. 140–250°, infrared chloroform, 1783 cm.$^{-1}$ and 1750 cm.$^{-1}$ ($\Delta^{\alpha,\beta}$-butenolide). When the heating was extended to 60 hr., an amorphous residue was obtained; infrared absorption at 1750 cm.$^{-1}$ with no $\Delta^{\beta,\gamma}$-butenolide band at 1783 cm.$^{-1}$

Alkaline hydrolysis of II. To 500 mg. of II was added 20 ml. of 6*N* sodium hydroxide and the mixture was heated under reflux for 3 hr. The reaction mixture was neutralized with 20% hydrochloric acid and the solid was collected. Crystallization from ethyl acetate gave 444 mg. (84%) of 2-phenacyl-3,3-diphenylpropionic acid (VIII), m.p. 185–186°. Infrared absorption at 1705 cm.$^{-1}$ and 1680 cm.$^{-1}$

Anal. Calcd. for $C_{23}H_{20}O_3$: C, 80.21; H, 5.85. Found: C, 80.09; H, 6.01. Mol. wt. calcd. 344. Found: 342 (neut. equiv.).

When VIII was heated under reflux with acetic anhydride (saturated with sodium acetate) for 3 hr., a solid melting at 280° was obtained, which showed no depression when mixed with an authentic sample of III.

Reaction of II *with hydrogen. In ethanol.* Five hundred milligrams of II, dissolved in 250 ml. of ethanol, was treated with hydrogen under 40 p.s.i. for 3 hr. using 5% palladium on charcoal catalyst. When the solvent was removed by air blowing, a residue was obtained which was taken up in a mixture of petroleum ether and ethyl acetate (10:1) and placed in a refrigerator for several days. There was obtained 208 mg. (41%) of 2-benzhydryl-4-phenylbutyric acid (IX), m.p. 135–136°. Infrared absorption at 1700 cm.$^{-1}$

Anal. Calcd. for $C_{23}H_{22}O_2$: C, 83.60; H, 6.71. Found: C, 83.42; H, 6.63. Mol. wt. calcd. 330. Found: 327 (neut. equiv.).

When methanol was used as a solvent, IX was obtained in 40% yield.

Clemmensen reduction[12] (zinc amalgam and concentrated hydrochloric acid) of VIII yielded a substance, m.p. 135°, which gave no melting point depression with an authentic sample of IX.

In acetic acid. Five hundred milligrams of II, dissolved in 150 ml. of glacial acetic acid, was hydrogenated for 3 hr. under 40 p.s.i. using 5% palladium on charcoal catalyst. Evaporation of the solvent by air blowing yielded a residue which was dissolved in methanol and refrigerated for several days to give 226 mg. (45%) of α-benzhydryl-γ-phenyl-γ-butyrolactone (X), m.p. 125–127°. Infrared absorption at 1758 cm.$^{-1}$

Anal. Calcd. for $C_{23}H_{20}O_2$: C, 84.14; H, 6.14. Found: C, 83.94; H, 6.04.

Compound X reacted with hydrogen in methanol to give a substance melting at 135° which showed no melting point depression when mixed with an authentic sample of IX.

Alkaline hydrolysis of X. To 180 mg. of X was added 20 ml. of 6*N* sodium hydroxide and the mixture was heated under reflux for 3 hr. The reaction mixture was worked up in the usual manner to yield 130 mg. (68%) of 2-benzhydryl-4-hydroxy-4-phenylbutyric acid (XI), m.p. 145–148°. Recrystallization from chloroform yielded a white solid, m.p. 147–149°.

Anal. Calcd. for $C_{23}H_{22}O_3$: C, 79.74; H, 6.40. Found: C, 79.43; H, 6.09. Infrared absorption at 1700 cm.$^{-1}$ and 3500–3200 cm.$^{-1}$

When heated with acetic anhydride, XI gave a solid, melting at 125°, which did not depress the melting point of an authentic sample of X.

Reaction of I *with phenyllithium.* To 1.05 g. (0.15 g.-atom) of lithium, suspended in 50 ml. of dry ether, was added several milliliters of a bromobenzene-ether solution (7.9 ml., 0.075 mole bromobenzene in 25 ml. of ether).

The mixture was heated under reflux until reaction began and then the remainder of the bromobenzene solution was added at intervals so as to insure gentle reflux.

I (6.2 g., 0.025 mole), in 225 ml. of ether, was added in portions during a 15-min. period and then the mixture was heated under reflux for 0.5 hr. The reaction mixture was hydrolyzed with 8% sulfuric acid solution, the ether layer was separated, washed with water and dried over anhydrous magnesium sulfate. Evaporation of the ether solution by air blowing yielded an oil, which was dissolved in acetone and evaporated by air blowing until a substantial amount of white solid separated. Recrystallization from acetone yielded 5 g. (49%) of 1,1-diphenyl-2-phenacylcinnamyl alcohol (IV), m.p. 127–130°. Infrared absorption at 3460 cm.$^{-1}$ and 1695 cm.$^{-1}$

Anal. Calcd. for $C_{29}H_{24}O_2$: C, 86.11; H, 5.98. Found: C, 85.21; H, 6.59.

A narrow melting point range could not be duplicated in subsequent crystallizations. Attempted purification of IV by elution chromatography on alumina, failed. IV was un-

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(11) F. W. Schueler and C. Hanna, *J. Am. Chem. Soc.*, 73, 3528 (1951).

(12) *Org. Reactions*, I, 168 (1942).

stable at room temperature on prolonged standing or on heating, turning green in color. The attempted preparation of the 2,4-dinitrophenylhydrazone, oxime and semicarbazone of IV yielded only the dihydrofuran XII.

2,2,5-Triphenyl-3-benzylidene-2,3-dihydrofuran (XII). To 1 g. (0.0025 mole) of IV was added 30 ml. of a saturated solution of sodium acetate in acetic anhydride. The solution was heated on a steam bath for 5 hr., then extracted with ether. The ether extract was washed several times with water, dried over magnesium sulfate and evaporated to yield a yellow-green solid. The crude product was crystallized from ethanol to yield 0.6 g. (62%) of dihydrofuran as fluorescent yellow-green needles, m.p. 150–151.5°.

Anal. Calcd. for $C_{29}H_{22}O$: C, 90.14; H, 5.74. Found: C, 90.20; H, 5.87.

Acknowledgment. The authors are grateful to the National Science Foundation for financial support of this research (Grant No. NSF-G9985).

CHICAGO 16, ILL.

[CONTRIBUTION FROM THE UNIVERSITY OF NEW MEXICO AND BIOMEDICAL RESEARCH GROUP,[1] LOS ALAMOS SCIENTIFIC LABORATORY, UNIVERSITY OF CALIFORNIA]

Liquid Scintillators. IX. Synthesis of Some Aryl Substituted Phenanthrenes and Dihydrophenanthrenes, and Related *p*-Terphenyls and *p*-Quaterphenyls[2]

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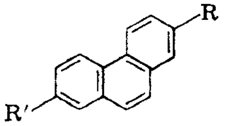
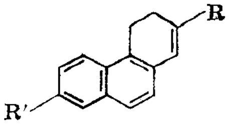
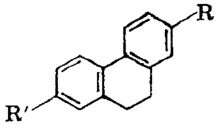
Received October 28, 1960

2-Phenylphenanthrene and 2-(4-biphenylyl)phenanthrene, synthesized *via* the corresponding 2-aryl-3,4-dihydrophenanthrenes, were converted to the related 2,2′-bis(hydroxymethyl)- and 2,2′-bis(methoxymethyl)-*p*-terphenyls and *p*-quaterphenyls as well as the 3-aryl-5,7-dihydrodibenz[c,e]oxepins and 2-aryl-9,10-dihydrophenanthrenes. Analogous 2″,3′-disubstituted *p*-quaterphenyls, 5,7-dihydro-3,9-diphenyldibenz[c,e]oxepin, 9,10-dihydro-2,7-diphenylphenanthrene, and 2,7-diphenylphenanthrene were prepared starting with *p*-quaterphenyl-2″,3′-dicarboxylic acid. Evaluation of these compounds as liquid scintillation solutes is reported in Paper X of this series.

In Paper VI of this series,[4] the synthesis of some aryl-substituted fluorenes was reported along with the evaluation of these compounds as liquid scintillators. We are herewith describing the synthesis of some related phenanthrene derivatives. The compounds of initial interest in this study were 2-phenylphenanthrene (Ia), 2-(4-biphenylyl)phenanthrene (Ib), and 2,7-diphenylphenanthrene (Ic) as well as their 9,10-dihydro derivatives (IIIa, IIIb, and IIIc). The 3,4-dihydrophenanthrenes, IIa and IIb, were also prepared for evaluation as liquid scintillator solutes.

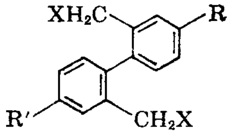




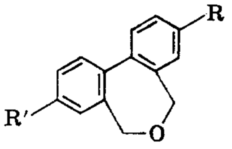


a. R′ = H, R = C_6H_5
b. R′ = H, R = 4-$C_6H_5C_6H_4$
c. R = R′ = C_6H_5

In the course of preparing the 9,10-dihydro derivatives, a number of interesting *p*-terphenyls (IVa, Va, and VIa) and *p*-quaterphenyls (IVb, IVc, Vb, Vc, VIb, and VIc) were synthesized from available intermediates.



IVa, b, c. X = OH
Va, b, c. X = OCH_3



VIa, b, c

2-Phenylphenanthrene (Ia) was prepared by the method described by Newman[5] and the 2-(4-biphenylyl) derivative Ib was obtained by a similar procedure, starting with phenylacetonitrile (series a) and 4-biphenylylacetonitrile (series b), respectively. The latter starting material was prepared in four steps from 4-biphenylcarboxylic acid which was reduced to 4-phenylbenzyl alcohol. This alcohol was converted to 4-phenylbenzyl bromide which, upon treatment with potassium cyanide, afforded 4-biphenylylacetonitrile. The alkylation of these arylacetonitriles was accomplished with 2-(1-naphthyl)ethyl bromide to give the corresponding 2-aryl-4-(1-naphthyl)butyronitriles, which were hydrolyzed to the substituted butyric acids. These were cyclized, *via* the acid chlorides, to the respective 2-aryl-1-oxo-1,2,3,4-tetrahydrophenanthrenes. Reduction of the ketones

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(1) Work done in part under the auspices of the U. S. Atomic Energy Commission.

(2) From the dissertation presented by Stephen P. Birkeland to the graduate faculty of the University of New Mexico in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) Graduate Research Assistant under Los Alamos Contract SC-5 with The University of New Mexico.

(4) M. D. Barnett, G. H. Daub, F. N. Hayes, and D. G. Ott, *J. Am. Chem. Soc.*, **81**, 4583 (1959).

(5) M. S. Newman, *J. Org. Chem.*, **9**, 518 (1944).