New Synthesis of
α-(Disubstituted Aminomethyl)-9-phenanthrenemethanols

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Abstract ☐ Treatment of 9-phenanthryllithium (I) with a variety of carbonyl compounds is described. Condensation of I with methyl N,N-dibutyloxamate gave N,N-dibutyl-9-phenanthreneglyoxylamide (III), which was reduced with sodium bis(2-methoxyethoxy)aluminum hydride to give α-[(N,N-dibutylamino)methyl]-9-phenanthrenemethanol (VI). Similarly, condensation of 3,6-bis(trifluoromethyl)-9-phenanthryllithium (II) with N,N-dibutyloxamate and N,N-diheptyloxamate gave, respectively, N,N-dibutyl- and N,N-diheptyl-3,6-bis(trifluoromethyl)-9-phenanthreneglyoxylamides (IV and V). Reduction of both carbonyl functions of IV and V simultaneously with diborane gave, respectively, α-[(N,N-dibutylamino)-methyl]- and α-[(N,N-diheptylamino)methyl]-3,6-bis(trifluoromethyl)-9-phenanthrenemethanols (VII and VIII).

Keyphrases ☐ α-Aminomethyl-9-phenanthrenemethanols—synthesis ☐ 9-Phenanthryllithiums—reactant, synthesis of α-aminomethyl-9-phenanthrenemethanols ☐ N,N-Disubstituted 9-phenanthreneglyoxylamides—synthesis, reduction ☐ Phenanthrenemethanols—synthesis

Halogen-containing α-(aminomethyl)-9-phenanthrenemethanols are active and curative against *Plasmodium berghei* in mice (1) and cause none of the photosensitization observed with many quinolinemethanols (1, 2). Phenanthrenemethanols are prepared by multistep syntheses (1, 3); in one method the amination of a phenanthrylethylene oxide can give a mixture of two isomers (4). The preparation of two 3,6-bis(trifluoromethyl)phenanthrenemethanols by a shorter and unambiguous route resulted from an investigation of the condensation reactions of 9-phenanthryllithium with various carbonyl compounds[1].

DISCUSSION

The lithiation of 9-bromophenanthrene to give 9-phenanthryllithium (I) was described previously (6), and a suspension of I in ether was used in most of the condensation reactions described here. As expected, carbonation of I gave 9-phenanthroic acid (71%) (6) and phenanthrene (20%)[2]. Treatment of I with carbobenzoxy chloride at −20° readily gave benzyl 9-phenanthroate, which was not isolated but was saponified to give 9-phenanthroic acid. In contrast, the reaction of I with ethyl oxalyl chloride gave a complex mixture, the mass spectrum of which indicated the presence of ethyl 9-phenanthreneglyoxylate (9-C₁₄H₉COCO₂C₂H₅) and mainly higher molecular weight structures. Similarly, the condensation of I with either ethyl N,N-dibutylglycinate (8, 9) or the hydrochloride of N,N-dibutylglycyl chloride (10, 11) at −70° appeared to give a mixture of phenanthrene, 9-phenanthrol, and 9,9'-biphenanthryl [9,9'-(C₁₄H₉)₂], but none of the desired ketone 9-C₁₄H₉-COCH₂N(C₄H₉)₂. Also, treatment of I with (diethylamino)acetone to give α-(diethylaminomethyl)-α-methyl-9-phenanthrenemethanol [9-C₁₄H₉C(OH)(CH₃)CH₂N(C₂H₅)₂] over a temperature range of from −50 to +35° was unsuccessful[3]. However, successful reactions were obtained by condensation of I at −70° with p-(N,N-

dimethylamino)benzaldehyde to give α-(p-N,N-dimethylanilino)-9-phenanthrenemethanol [9-C₁₄H₉CH(OH)C₆H₄N(CH₃)₂-p] and with chloroacetaldehyde, prepared by distillation of its cyclic trimer (13), to give α-(chloromethyl)-9-phenanthrenemethanol [9-C₁₄H₉CH-(OH)CH₂Cl].

These aldehyde condensations then prompted the preparation of N,N-(dibutylamino)acetaldehyde by hydrolysis of its acetal (14) in dioxane with hydrochloric acid. The NMR spectrum in CDCl₃ indicated that the product was a mixture of the aldehyde and two other components, probably its hydrate and a polymeric form. The condensation of this mixture with I in tetrahydrofuran at −10° gave mainly phenanthrene, but the mass spectrum also indicated the presence of α-[(N,N-dibutylamino)methyl]-9-phenanthrenemethanol [9-C₁₄H₉CH(OH)CH₂N(C₄H₉)₂] (VI) and 9,9'-biphenanthryl. The amination of α-(chloromethyl)-9-phenanthrenemethanol already described to give VI was not attempted because of the development of a more practical route to this compound.

The best method found for the preparation of phenanthrenemethanols involves the condensation of I with methyl N,N-dibutyloxamate to give N,N-dibutyl-9-phenanthreneglyoxylamide [C₁₄H₉-9-COCON(C₄H₉)₂] (III) followed by simultaneous reduction of both carbonyl functions with Na(CH₃OCH₂CH₂O)₂AlH₂ to give VI, isolated in good yield as the sulfate (3).

Attention was then directed toward the conversion of 9-bromo-3,6-bis(trifluoromethyl)phenanthrene[4] to the corresponding 9-phenanthryllithium compound (II). Treatment of an ether solution of this 9-bromophenanthrene with n-butyllithium gave a red solution, which was shown to contain II by carbonation to give a good yield of 3,6-bis(trifluoromethyl)-9-phenanthroic acid (1) and 3,6-bis(trifluoromethyl)phenanthrene. A similar solution of II was condensed with methyl N,N-dibutyloxamate at −70° to give the corresponding phenanthrene and mainly the N,N-dibutyl-9-phenanthreneglyoxylamide (IV), which was obtained pure by column chromatography. The reduction of both carbonyl functions of IV was effected with Na(CH₃OCH₂CH₂O)₂AlH₂; however, this reagent also caused partial reductive defluorination of the trifluoromethyl groups. In addition, both chromatographic and spectral data indicated the presence of phenanthroic acids, presumably resulting from cleavage between the carbonyl groups of IV in the basic medium. The successful reduction of IV to the corresponding phenanthrenemethanol (VII) was effected with diborane. A higher overall yield of VII was obtained by treatment of the described mixture of IV and the by-product, 3,6-bis(trifluoromethyl)phenanthrene, with this reducing reagent. Similarly, the condensation of II with N,N-diheptyloxamate gave the 9-phenanthreneglyoxylamide (V), which was not purified but reduced with diborane to give VIII directly (Scheme I).

EXPERIMENTAL[5]

N,N-(Dibutylamino)acetaldehyde Hydrochloride—Concentrated hydrochloric acid (3.4 ml.) was added dropwise to a cold solution of N,N-dibutylaminoacetaldehyde diethyl acetal (5.00 g., 20.4 mmoles) in dioxane. The resulting solution was covered with nitrogen and stirred for 20 hr. at room temperature, with formation of an amber color within the first 2 hr. The solution was frozen in dry ice and lyophilized for 60 hr. The residue was a viscous amber syrup which became a light-brown semisolid upon prolonged drying *in vacuo* over phosphorus pentoxide, yielding 5.2 g. The NMR spectrum of this
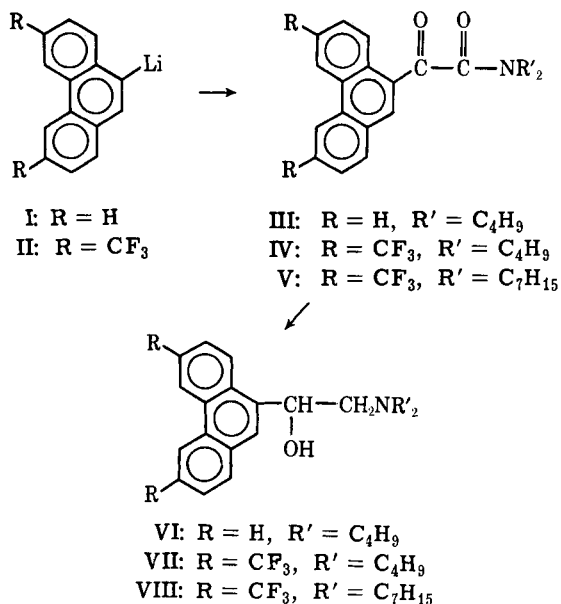
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[1] A preliminary report of part of this work appeared previously (5).
[2] Presumably this product is formed from the reaction of I with the solvent (7).
[3] Condensation of this ketone with a Grignard compound was reported (12).

[4] The authors express appreciation to Drs. T. R. Sweeney and R. E. Strube of the Walter Reed Army Institute of Research for this material, prepared by the method of Ohno and Tsuji (15) from the corresponding phenanthroic acid (1).
[5] Melting points were determined on a Mel-Temp apparatus.

I: R = H
II: R = CF₃

III: R = H, R' = C₄H₉
IV: R = CF₃, R' = C₄H₉
V: R = CF₃, R' = C₇H₁₅

VI: R = H, R' = C₄H₉
VII: R = CF₃, R' = C₄H₉
VIII: R = CF₃, R' = C₇H₁₅

Scheme I

residue in $CDCl_3$ (tetramethylsilane) indicated the presence of the acetaldehyde [17%, δ ~9.8 (CHO)] and two other compounds, probably its hydrate and a polymeric form [δ ~5.5, 5.2(—OC(—)HO—)]. This sample, without further purification, was condensed with I.

Methyl *N,N*-Dibutyloxamate—A solution of dimethyl oxalate (50.0 g., 423 mmoles) and dibutylamine (54.7 g., 423 mmoles) in methanol (150 ml.) was stirred under nitrogen at room temperature for 24 hr., refluxed for 36 hr., and concentrated under reduced pressure to give a mixture of white crystalline solid and viscous yellow oil. The solid was collected by filtration, washed with hexane, and dried *in vacuo* over phosphorus pentoxide at 65°, yielding 1.37 g., m.p. 197–200°. This product was identified by its elemental analysis and IR spectrum as the bis(dibutyl)amine [bis-(C₄H₉)₂NH] salt of oxalic acid. The yellow oil was distilled *in vacuo* through a short Vigreaux column, yielding 64.0 g. (70.4%), b.p. 104–108°/1.2 mm. TLC showed the presence of both dimethyl oxalate and diphenanthryl-amine [(C₉H₁₄)₂NH]. The colorless oil was redistilled *in vacuo*, yielding 58.4 g. (64.2%), b.p. 104–105°/1.0 mm.

Anal.—Calc. for C₁₁H₂₁NO₃: C, 61.37; H, 9.83; N, 6.51. Found: C, 61.14; H, 9.70; N, 6.41.

Methyl *N,N*-Diheptyloxamate—A solution of dimethyl oxalate (39.1 g., 331 mmoles) and diheptylamine (70.6 g., 331 mmoles) in methanol (150 ml.) was refluxed under a nitrogen atmosphere for 64 hr. and concentrated under reduced pressure to give a mixture of a viscous yellow oil and white crystalline solid. The solid (1.45 g.) was removed by filtration, and the clear yellow oil was distilled *in vacuo*. After a few drops of colorless distillate was collected (oil bath 115–120°/0.02–0.03 mm.), the pressure rose quickly to ~2 mm. and distillation ceased. The distillate was identified as *N,N*-diheptylmethylamine [(C₇H₁₅)₂NCH₃] by its IR and mass spectrum (M⁺ = 227). The clear, yellow pot residue (79.6 g.) was chromatographed on a silica gel H column (1.2 kg.) which was eluted with hexane–chloroform (2:1). The first major fraction was the desired oxamate ester, obtained as a clear, chromatographically homogeneous oil by evaporation of the solvent, yielding 20.6 g. (21%).

Anal.—Calc. for C₁₇H₃₃NO₃: C, 68.19; H, 11.10; N, 4.68. Found: C, 67.99; H, 10.92; N, 4.40.

A second fraction (5.8 g.) contained mainly the oxamate ester, but the sample was contaminated with a small amount of *N,N*-diheptylformamide [(C₇H₁₅)₂NCHO] as shown by its mass spectrum. The third fraction (2.1 g.) was chromatographically homogeneous (C₇H₁₅)₂NCHO. The fourth major fraction was collected as several portions from a diffuse, slow-moving band on the column, total weight 7.2 g. TLC and a mass spectrum of the largest portion indicated the presence of diheptylamine, *N,N*-diheptylmethylamine, and(C₇H₁₅)₂NCOCO₂H. The formation of the by-products was attributed to the thermal degradation of the desired oxamate when the distillation of the crude product was attempted.

9-Phenanthryllithium (I) (6)—Under a nitrogen atmosphere, a 21.3% (w/w) solution of butyllithium in hexane (8.6 ml., 19.5 mmoles, 25% excess) was added by hypodermic syringe to an ice-cold solution of 9-bromophenanthrene (4.00 g., 15.6 mmoles) in dry ether (60 ml.). The resulting suspension was centrifuged, the ether was decanted, and the solid I was transferred under nitrogen with the aid of dry ether (120 ml.) to the reaction flask. A suspension of I prepared in this manner was used in the following condensation reactions.

9-Phenanthroic Acid—*Procedure A*—A suspension of I in ether (30 ml.) prepared from 9-bromophenanthrene (1.0 g., 3.9 mmoles) was cooled to −20° in a dry ice-acetone bath and treated with carbobenzoxy chloride (0.67 g., 3.9 mmoles). The resulting solution was allowed to warm slowly to room temperature, during which time a large amount of lithium chloride deposited. Water (50 ml.) was added to the mixture, and the ether layer was separated, washed with water, dried over sodium sulfate, and evaporated *in vacuo* to give a pale-yellow viscous oil, yielding 1.2 g. A solution of this oil and potassium hydroxide pellets (10 g.) in 90 ml. of ethanol was refluxed for 2 hr. and evaporated to dryness *in vacuo*. The residue was triturated with water (50 ml.), and the resulting solution was filtered from 0.47 g. of dark-brown resinous matter. The filtrate was acidified to pH 4 with concentrated sulfuric acid, and the crystalline precipitate was collected by filtration and dried *in vacuo* over phosphorus pentoxide, yielding 0.29 g. (33.5%), m.p. 253–255° with charring [lit. (6) m.p. 251–252°, 255–257°].

Procedure B—A suspension of I in ether was poured over crushed dry ice to give a 71% yield of 9-phenanthroic acid, m.p. 252–255°, and a 20% yield of crude phenanthrene.

α-(*p-N,N*-Dimethylanilino)-9-phenanthrenemethanol Monohydrochloride—A suspension of I in ether (60 ml.) prepared from 9-bromophenanthrene (2.0 g., 7.8 mmoles) was cooled to −70° under a nitrogen stream and then treated dropwise with a solution of *p*-(*N,N*-dimethylamino)benzaldehyde (1.2 g., 7.8 mmoles) in ether (30 ml.). The resulting suspension was allowed to warm to room temperature and rapidly developed a bright-yellow color near 0°. The suspension was refluxed gently for 4 hr., cooled, and poured into cold water (100 ml.). The ether layer was washed with cold saturated sodium bisulfite solution (200 ml.) and water (2 × 100 ml.), dried over sodium sulfate, and evaporated to dryness to give a soft solid, yielding 1.90 g. This material was precipitated as the hydrochloride salt by bubbling dry hydrogen chloride gas into a solution of the crude solid in ether (200 ml.). The hygroscopic, violet-colored solid was collected by filtration under nitrogen and dried over phosphorus pentoxide *in vacuo*, yield 1.31 g. (46.2%). To prepare a sample free of the violet color, a solution of the solid in ethanol (50 ml.) was treated with charcoal, filtered through diatomaceous earth[6], and diluted with ether until precipitation was complete. The nearly colorless solid was collected under nitrogen and dried *in vacuo* over phosphorus pentoxide. However, when this sample was dried, it reassumed its violet color, yielding 0.31 g. (10.9%), melting point sintered and decomposed above 140°.

Anal.—Calc. for C₂₃H₂₁NO·HCl: C, 75.92; H, 6.09; N, 3.85; Cl, 9.74. Found: C, 75.71; H, 5.91; N, 4.03; Cl, 9.54.

α-(Chloromethyl)-9-phenanthrenemethanol—A suspension of I in ether (100 ml.) prepared from 9-bromophenanthrene (4.00 g., 15.6 mmoles) was transferred to a three-necked flask fitted with a nitrogen inlet, condenser, and a connecting tube bent at a 105° angle. The latter was also attached to a small round-bottom flask containing the solid cyclic trimer of chloroacetaldehyde (2.5 g., 31.8 mmoles as the aldehyde, 100% excess) (13). The ether suspension was cooled to −70° in dry ice; anhydrous chloroacetaldehyde was distilled from the side flask into the reaction mixture by application of direct heat from a burner. When the distillation was complete (~30 min.), the greenish-yellow suspension was allowed to warm to room temperature. Ice water (100 ml.) was added, and the aqueous layer was separated and extracted with ether (150 ml.). The combined ether extract was washed by shaking with ice-cold saturated sodium bisulfite solution (100 ml.) and cold water (3 × 100 ml.), dried over sodium sulfate, and evaporated *in vacuo* to give a spongy beige solid, yielding 4.0 g. This crude material was dissolved in ether (150 ml.), and the solution was diluted to a volume of 500 ml. with hexane and refrigerated overnight. The deposit of tan needles was collected by filtration, washed with cold hexane, and

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[6] Celite.

dried *in vacuo* over phosphorus pentoxide, yielding 1.69 g. (42.2%), m.p. 139–140°.

Anal.—Calc. for $C_{16}H_{13}ClO$: C, 74.86; H, 5.10; Cl, 13.81. Found: C, 74.75; H, 5.13; Cl, 13.68.

A second crop of colorless crystals was obtained by treating the filtrate from the first crop with charcoal, evaporating the solvents, and recrystallizing the residue from fresh ether–hexane, yielding 0.38 g. (9.5%), m.p. 138–140°. The total yield was 2.07 g. (51.7%).

N,N-Dibutyl-9-phenanthreneglyoxylamide (III)—A suspension of I in ether (120 ml.) prepared from 9-bromophenanthrene (4.00 g., 15.6 mmoles) was cooled under a stream of nitrogen to −70° in dry ice. A solution of freshly distilled methyl *N,N*-dibutyloxamate (3.36 g., 15.6 mmoles) in ether (25 ml.) was added in a rapid stream, and the resulting clear yellow solution was stirred at −70° for 30 min. and then at room temperature. After 1.5 hr. the reaction mixture began to deposit a fine granular white solid. After 2 hr. the suspension was treated with cold water (100 ml.) and the ether layer was separated. The latter was diluted to a volume of 250 ml. with ether and washed with water (3 × 100 ml.), dried over sodium sulfate, and evaporated under reduced pressure to a clear yellow oil, yielding 5.30 g. (94%). The crude oil was dissolved in hexane–chloroform (2:1), and the solution was poured onto a silica gel H column (150 g.). Elution with hexane–chloroform (2:1) and evaporation of the solvent gave three major fractions: (*a*) phenanthrene, yield 0.24 g., m.p. 95–96° (after recrystallization from ethanol); (*b*) III, yield 4.40 g. (78%) as a pale-pink oil that solidified slowly upon prolonged drying *in vacuo;* and (*c*) mixture of III and unreacted methyl *N,N*-dibutyloxamate (0.60 g.). A solution of fraction *b* in warm methanol (150 ml.) was treated with charcoal and filtered through diatomaceous earth followed by evaporation of the solvent, yielding 3.37 g. (59.7%), m.p. 61–62°.

Anal.—Calc. for $C_{24}H_{27}NO_2$: C, 79.74; H, 7.53; N, 3.88. Found: C, 79.76; H, 7.48; N, 4.06.

In another run the product was also purified by column chromatography. With chloroform–hexane (1:1) as the elution solvent, the yield of homogeneous, waxy material was 2.3 g. (40.8%). This solvent caused partial overlapping of the bands of III and the trailing oxamate ester. Thus, an additional 1.8 g. (31.9%) of the desired product contaminated (TLC) with the oxamate ester was obtained. The total yield was 4.1 g. (72.7%).

3,6-Bis(trifluoromethyl)-9-phenanthroic Acid—Under a nitrogen atmosphere, a 21.3% (w/w) solution of *n*-butyllithium in hexane (1.2 ml., 2.8 mmoles, 10% excess) was added by hypodermic syringe to a slightly cooled (~10°) solution of 9-bromo-3,6-bis(trifluoromethyl)phenanthrene (1.0 g., 2.5 mmoles) in dry ether (75 ml.) with instantaneous formation of a clear, wine-red solution of II. This solution was stirred under nitrogen with ice cooling for 30 min. and then poured onto a large excess of freshly crushed dry ice. After evaporation of the ether and carbon dioxide, the brick-red residue was stirred with water (200 ml.) containing 0.25 ml. of 50% sodium hydroxide solution. The insoluble matter was collected by centrifugation; the sediment was washed by trituration with water, centrifugation, and decantation. The combined washes were acidified with excess concentrated hydrochloric acid, and the precipitated gelatinous solid was collected by filtration, washed with water, and dried *in vacuo* over phosphorus pentoxide, yielding 0.56 g. (61.6%), m.p. 263–266° with prior sintering. The crude acid was reprecipitated under the same conditions with charcoal treatment, washed with water, and dried *in vacuo* over phosphorus pentoxide at 65°, yielding 0.36 g. (39.5%), m.p. 268–269° with prior sintering [lit. (1) m.p. 272–273°].

Anal.—Calc. for $C_{17}H_8F_6O_2$: C, 57.00; H, 2.25; F, 31.82. Found: C, 57.05; H, 2.08; F, 31.56.

A portion of the dark-red, base-insoluble centrifugation sediment (0.24 g.) was sublimed *in vacuo* at 40–50°. The pale-yellow crystalline sublimate was identified as 3,6-bis(trifluoromethyl)phenanthrene by its mass spectrum, m.p. 124–126°.

N,N-Dibutyl-3,6-bis(trifluoromethyl)-9-phenanthreneglyoxylamide (IV)—Under a nitrogen atmosphere, a 21.3% (w/w) solution of *n*-butyllithium in hexane (4.9 ml., 11 mmoles, 10% excess) was added by hypodermic syringe to a solution of 9-bromo-3,6-bis(trifluoromethyl)phenanthrene (4.0 g., 10 mmoles) in dry ether (300 ml.) that had been cooled to −70° in a dry ice-acetone bath. After stirring the wine-red solution for 10 min., a solution of freshly distilled methyl *N,N*-dibutyloxamate (2.4 g., 11 mmoles, 10% excess) in ether (25 ml.) was added rapidly. External cooling was removed,

and the reaction mixture was stirred at room temperature for 4 hr. The dark-orange solution was treated with cold water (100 ml.), and the ether layer was washed with water (3 × 100 ml.), dried over sodium sulfate, and evaporated under reduced pressure to give an amber semisolid residue, yielding 4.8 g. This material was dissolved in hexane–chloroform (2:1) and poured onto a silica gel H column (175 g.). Elution with the same solvent gave four major fractions: (*a*) a pale-yellow solid identified as 3,6-bis(trifluoromethyl)phenanthrene, yield 0.83 g. (26%), m.p. 122–123°; (*b*) an unidentified waxy orange solid, yield 0.30 g., m.p. 170–175°; and (*c*) an off-white solid of IV, yield 2.40 g. (47.3%), m.p. 149–150°.

Anal.—Calc. for $C_{26}H_{25}F_6NO_2$: C, 62.77; H, 5.07; N, 2.82. Found: C, 62.61; H, 4.84; N, 2.63.

Fraction *d* was a chromatographically complex mixture consisting mainly of unreacted oxamate ester, yielding 0.83 g.

α-[(N,N-Dibutylamino)methyl]-9-phenanthrenemethanol Hydrogen Sulfate (VI)—Procedure A—A solution of III (1.42 g., 3.90 mmoles) in ether (30 ml.) was added dropwise at room temperature to a 70% benzene solution of $Na(CH_3OCH_2CH_2O)_2AlH_2$ (4.40 ml., 15.7 mmoles) that had been diluted with ether (30 ml.). The pale-yellow mixture was stirred under nitrogen for 1 hr. and then refluxed for 5 min. and treated dropwise with ice water (10 ml.). The sodium aluminate that precipitated was dissolved by the addition of 50% sodium hydroxide solution (15 ml.). The aqueous layer was extracted with ether (75 ml.), and the combined ether layers were washed with water (3 × 120 ml.), dried over sodium sulfate, and evaporated under reduced pressure to give a pale-yellow oil. A solution of the oil in ether (25 ml.) was acidified with a slight excess of sulfuric acid. The ether was evaporated, and the residual oil was washed by trituration with hexane (150 ml.) and decantation. This material was dissolved in ethanol (60 ml.), and the filtered solution was diluted slowly with ether (600 ml.). The granular white deposit that formed after 1 hr. of stirring was collected by filtration and dried *in vacuo* over phosphorus pentoxide, yielding 40 mg., m.p. 233–235° dec. with prior sintering. This material was tentatively identified as an ethylene derivative $[C_{14}H_9—CH=CH—N(C_4H_9)_2 \cdot H_2SO_4]$, based on mass spectral analysis (M^+ = 331).

The ethanol–ether filtrate was stirred overnight to deposit a granular white solid of VI·H_2SO_4, yielding 0.29 g. (47%), m.p. 115–117°. TLC showed that some of the by-product obtained in the first crop was present as a trace impurity.

Anal.—Calc. for $C_{24}H_{31}NO \cdot H_2SO_4$; C, 64.41; H, 7.43; N, 3.13. Found: C, 64.30; H, 7.10; N, 2.97.

Procedure B—A suspension of I in tetrahydrofuran (40 ml.) prepared from 9-bromophenanthrene (15.4 g., 60.0 mmoles) was cooled to −10° and treated rapidly with a solution in tetrahydrofuran (75 ml.) of the crude product (3.60 g.) obtained from the hydrolysis of *N,N*-dibutylaminoacetaldehyde diethyl acetal in dioxane. The resulting dark solution was stirred at −10° for 1 hr., at room temperature for 20 hr., and at 60–65° on the water bath for 5 hr. The cooled solution was evaporated to dryness *in vacuo*, and the residue was dissolved in ether (200 ml.). The solution was shaken with ice-cold water (4 × 100 ml.), dried over sodium sulfate, and evaporated *in vacuo* to give a mixture of tan solid and viscous oil, yielding 12.4 g. Precipitation of the desired compound as the amine hydrochloride salt by bubbling dry hydrogen chloride gas into a solution of the crude mixture in ether (250 ml.) was unsuccessful. The solution was evaporated, and the dark gummy residue was triturated with hexane (3 × 200 ml.). Evaporation of the hexane gave solid phenanthrene, yielding 7.1 g., m.p. 94–96° (after recrystallization from ethanol). Mass spectral analysis of the crude hexane-insoluble residue (5.7 g.) showed the presence of the desired phenanthrenemethanol (M^+ = 349) and a prominent peak attributed to 9,9′-biphenanthryl (M^+ = 354).

α-[(N,N-Dibutylamino)methyl]-3,6-bis(trifluoromethyl)-9-phenanthrenemethanol Monohydrochloride (VII)—Procedure A—Under an atmosphere of dry nitrogen, a 21.3% (w/w) solution of *n*-butyllithium in hexane (7.40 ml., 16.8 mmoles, 10% excess) was added by hypodermic syringe to an ice-cold solution of 3,6-bis(trifluoromethyl)-9-bromophenanthrene (6.00 g., 15.2 mmoles) in dry ether (400 ml.). After 10 min. the dark-red solution was cooled to −70° in a dry ice-acetone bath and then treated in a rapid stream with a solution of methyl *N,N*-dibutyloxamate (3.62 g., 16.8 mmoles, 10% excess) in dry ether (50 ml.). The resulting orange solution was stirred at room temperature for 2 hr., heated at reflux for 15 min., cooled, and then treated with cold water (150 ml.). The organic

layer was washed with water (2 × 150 ml.), dried over sodium sulfate, and evaporated under reduced pressure to a crusty orange semisolid which was dried briefly by oil pump evacuation. The orange material was dissolved in dry tetrahydrofuran (100 ml.), and the solution was added rapidly dropwise to an ice-cold solution of 1 M BH$_3$ in tetrahydrofuran (80 ml.) diluted with tetrahydrofuran (100 ml.). The resulting solution was refluxed for 1 hr., cooled in ice, and treated dropwise with 6 N HCl (50 ml.) with vigorous hydrogen gas evolution. The turbid mixture was evaporated to dryness *in vacuo*, yielding 7.2 g. The gummy residue was triturated thoroughly with cold water (2 × 150 ml.). The residue was dissolved in ethanol (250 ml.), and the solution was treated with charcoal, filtered, and evaporated to dryness. The yellow gum was dissolved in chloroform (300 ml.); water (200 ml.) was added and, with intermittent vigorous stirring, the aqueous layer was adjusted to pH 7–8 (paper) by portionwise addition of solid sodium bicarbonate. The chloroform layer was washed with water (200 ml.), dried over sodium sulfate, and evaporated *in vacuo* to a soft-yellow solid, yielding 7.1 g. This material was dissolved in dry ether (500 ml.), and dry hydrogen chloride gas was bubbled in slowly, but no precipitate formed. After evaporation of the ether and partial evaporation of a second 500-ml. portion, crystallization of a granular white solid occurred. After standing for 2 hr., the solid was collected by filtration, washed with ether, and dried *in vacuo* over phosphorus pentoxide, yielding 3.70 g. (47%), m.p. 210–213° dec. with prior sintering. This solid was dissolved in warm ethanol (10 ml.), and the solution was added to dry ether (500 ml.) to deposit long white needles upon stirring for 18 hr. at room temperature. Concentration of the filtrate from the first crop and prolonged stirring gave a second crop of white solid with identical melting point, total yield 3.05 g. (38.6%), m.p. 217–219° dec. [lit. (1) m.p. 221–233.5°]. The sample was chromatographically homogeneous.

Anal.—Calc. for C$_{26}$H$_{29}$F$_6$NO·HCl: C, 59.83; H, 5.79; N, 2.68. Found: C, 59.81; H, 5.68; N, 2.56.

Procedure B—Under an atmosphere of dry nitrogen, a solution of 3,6-bis(trifluoromethyl)-N,N-dibutyl-9-phenanthreneglyoxylamide (0.50 g., 1.0 mmole) in dry, freshly distilled tetrahydrofuran (20 ml.) was added dropwise during 15 min. to an ice-cold solution of 1 M BH$_3$ in tetrahydrofuran (4 ml.) diluted with dry tetrahydrofuran (25 ml.). The initially bright-yellow solution was refluxed gently under nitrogen for 1 hr. with complete loss of color after 10 min. The solution was cooled in ice and treated dropwise with 6 N HCl (25 ml.) with evolution of hydrogen. Most of the tetrahydrofuran was removed by atmospheric distillation from a hot water bath. The turbid aqueous residue was diluted with water (100 ml.), and the mixture was adjusted to pH 5–6 (paper) by portionwise addition of solid sodium bicarbonate. The mixture was extracted with chloroform (3 × 100 ml.), and the extract was dried over sodium sulfate and evaporated to give a nearly colorless semisolid. This residue was dissolved in ethanol (10 ml.), and 2 N ethanolic HCl (1.0 ml.) was added to the solution. Dilution with ether (300 ml.) and refrigeration gave a deposit of white solid which was collected by filtration, washed with ether, and dried *in vacuo* over phosphorus pentoxide at 78°, yielding 0.16 g. (31%), m.p. 213–215° dec. with prior sintering.

Concentration of the filtrate from the first crop gave successive crops of 0.13 and 0.04 g., m.p. 211–213° and 212–214°, respectively. The total yield of product from the reaction was 0.33 g. (64%).

α-[(N,N-Diheptylamino)methyl]-3,6-bis(trifluoromethyl)-9-phenanthrenemethanol (VIII)—Under an atmosphere of dry nitrogen, a 21.3% (w/w) solution of n-butyllithium in hexane (4.2 ml., 9.6 mmoles, 5% excess) was added by hypodermic syringe to a suspension of 9-bromo-3,6-bis(trifluoromethyl)phenanthrene (3.6 g., 9.2 mmoles) in dry ether (150 ml.) that had been cooled to −10° in an ice-salt bath. The resulting dark-red solution was stirred at −10° for 10 min., cooled to −70° in a dry ice-acetone bath, and then treated with a solution of methyl N,N-diheptyloxamate (2.9 g., 9.6 mmoles, 5% excess) in dry ether (50 ml.). The orange-red solution was stirred at room temperature for 2 hr., refluxed for 15 min., cooled, and treated with cold water (200 ml.). The ether layer was washed with water (200 ml.), dried over sodium sulfate, and evaporated *in vacuo* to give V as a white solid colored slightly with

an orange-red impurity, crude yield 5.3 g. (99%). A solution of this solid in dry, freshly distilled tetrahydrofuran (50 ml.) was added dropwise during 15 min. to an ice-cold solution of 1 M BH$_3$ in tetrahydrofuran (60 ml.). After 15 min. at 0°, the solution was refluxed for 1 hr., cooled in ice, and treated dropwise with cold 6 N HCl (50 ml.) with vigorous evolution of hydrogen. The turbid mixture was evaporated to dryness *in vacuo*. The gummy residue was dissolved in chloroform (200 ml.); water (200 ml.) was added and, with vigorous intermittent stirring, the aqueous layer was adjusted to pH 7–8 (paper) by portionwise addition of solid sodium bicarbonate. The chloroform layer was washed with water (2 × 100 ml.), dried over sodium sulfate, and evaporated to give a clear yellow oil, yielding 5.2 g. Chromatography of this oil on a silica gel column [250 g., eluted with chloroform–hexane (2:1)] gave an unidentified fast-moving component (white waxy semisolid, 1.43 g.) and VIII as a clear yellow oil, yielding 3.57 g. (69.1%). TLC showed that the oil was contaminated with the fast-moving component. The hydrochloride salt of the phenanthrenemethanol could not be obtained in solid form by treatment of a solution of the oil in ethanolic hydrochloric acid with ether. The free-base form of the oil was passed through a second silica gel column under the same conditions as already described to yield the fast-moving component (0.57 g.) and VIII as an orange oil which partially solidified after drying by oil pump evacuation, yielding 2.00 g. (38.7%); mass spectrum, M$^+$ = 569, (M − 1)$^+$ = 568. A small portion of this sample was dried *in vacuo* over phosphorus pentoxide at 65° for 1 hr., m.p. 49–50°.

Anal.—Calc. for C$_{32}$H$_{41}$F$_6$NO: C, 67.47; H, 7.25; N, 2.46. Found: C, 67.28; H, 7.09; N, 2.31.

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