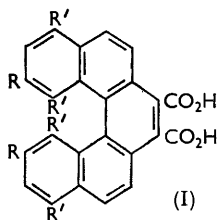


663. *Some Dibenzophenanthrenes Substituted in the Interfering Positions.*

By H. S. BLAIR, MALCOLM CRAWFORD, J. M. SPENCE, and V. R. SUPANEKAR.

2'',3'-Dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic acid has been resolved optically. 1',1'',4',4''-Tetramethoxy- and -tetraethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic acid in which intramolecular overcrowding due to substitution in the interfering positions is greater, have resisted all attempts at resolution. In the preparation of these compounds a mixture of palladium-charcoal and sulphur is a better dehydrogenating agent than either constituent separately.

THE dibromo-compound (I; R = Br, R' = H) was recently resolved.¹ The corresponding dimethoxy-compound (I; R = OMe, R' = H) is now found to be readily resolvable into optical isomers with a half-life period slightly greater than that of the active dibromo-analogue under similar conditions. The methoxyl group is less bulky than the bromine atom but its flexibility gives rise to a greater overlap area projected on the plane of the racemisation transition state, and the slower lower racemisation can be explained on this basis.



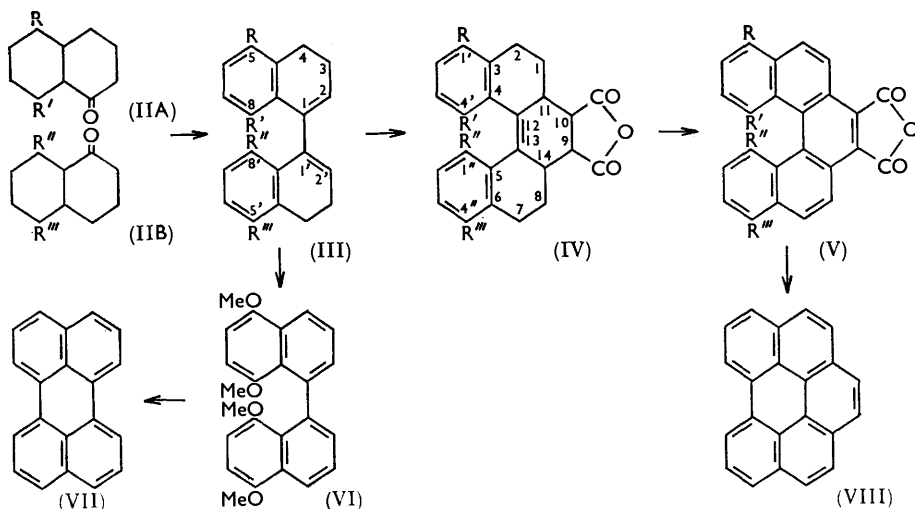
Most surprisingly the tetra-alkoxy-compounds (I; R = H, R' = OMe or OEt) are found to be preparable without difficulty in spite of the high degree of steric interference between neighbouring groups R' in (I) and groups R' and R'' in stages (III), (IV), and (V) of the synthesis. In view of the unexpected properties of the final anhydride (V) and acid (I), *e.g.*, colour, non-resolvability, and solubility of alkaloidal salts, the structures of intermediate stages in turn had to be firmly established, especially since the increasing steric pressure might well have resulted in the formation of abnormal products.

The starting tetralones (II) are known compounds.² When they undergo pinacol reduction the carbonyl groups in two molecules must approach closely to form the 1,1'-link. Carbon atom 8 and its substituent are in *ortho*-position to the carbonyl group. They

¹ Crawford, Mackinnon, and Supanekar, *J.*, 1959, 2807.

² Crawford and Supanekar, *J.*, 1960, 1985.

could possibly exert sufficient steric pressure to bring about a 1,2'- or 2,2'-linkage. This was found not to occur; the diene (III; R = R' = R'' = R''' = OMe) gave, on dehydrogenation, 5,5',8,8'-tetramethoxy-1,1'-binaphthyl (VI), which on distillation with zinc dust gave perylene (VII), identified by m. p. and ultraviolet absorption spectrum. The 1,1'-link in the diene (III) is thereby confirmed.



The diene (III) undergoes Diels-Alder addition of maleic anhydride readily. This is unexpected for two reasons, namely, (1) that the diene can assume a sufficiently planar conformation for this addition to take place, and (2) that the resulting highly strained adduct (IV) is a stable compound. Yet its colour and analysis support this structure. Its non-benzenoid double bond resisted ozonolysis. Dehydrogenation was also difficult. Bromine cannot be used because of substitution; lead tetra-acetate afforded products which were probably acetylated or acetoxyated; sulphur, selenium, and palladium gave poor yields of impure products. Curiously a mixture of sulphur and palladium-on-charcoal gave excellent yields of the anhydride (V) after 5—10 minutes' heating (cf. Johnson³). This dehydrogenating agent was found to be generally most effective.

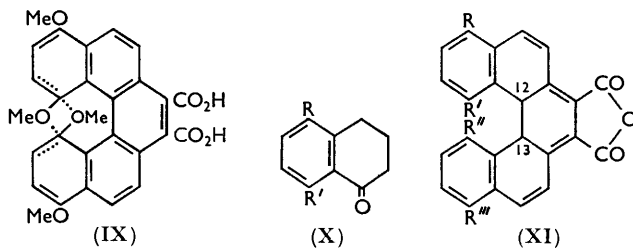
The anhydride (V) is a deep red or crimson substance. It contains the 3,4:5,6-dibenzo-phenanthrene system and not the 3,4:7,8- or other system arising possibly from distorted addition of maleic anhydride to the diene. This was clearly shown by partial demethylation and distillation of the product with zinc dust: 1,12-benzoperylene (VIII) was formed.

Wandering of alkoxy groups during the pinacol reduction of the ketone (II), during the Diels-Alder reaction or during the dehydrogenation, is considered to be extremely unlikely. If then, as appears, the acid (I; R = H, R' = OMe or OEt) has the structure shown not only ought it to be resolvable but the optical isomers would be expected to show considerable stability because of the high degree of blocking. All attempts at resolution having failed and the alkaloidal salts being so much more soluble than those of the dimethoxy- and dibromo-compounds already resolved, the possibility that the tetra-alkoxy-compounds contained some distinct structural feature was considered. Their more intense colour seemed to support this. Unsuccessful attempts⁴ to prepare a tetramethyl acid (I; R = H, R' = Me) indicate that the stability might reside in the alkoxy groups. A structure of the type (IX) might not only fit these findings but would impart symmetry and consequent non-resolvability. In it the two central methoxyl groups are

³ Johnson, *J.*, 1956, 4155.

⁴ Bell and Waring, *J.*, 1949, 2689.

equivalent. The possibility of such a structure was tested by the preparation of two unsymmetrically substituted compounds (V; R = R' = OMe, R'' = R''' = OEt) and (V; R = R'' = OMe, R' = R''' = OEt) which would be identical if the alkoxy groups R' = R'' were equivalently bound. A number of other isomers had also to be prepared and characterised to establish the structures of the required compounds.



The synthesis of these compounds was achieved by pinacol reduction of mixtures of the tetralones (X; R = R' = OMe and R = R' = OEt) on the one hand, and (X; R = OMe, R' = OEt and R = OEt, R' = OMe) on the other. The resulting diene mixtures of desired product plus the two symmetrical products were converted into their

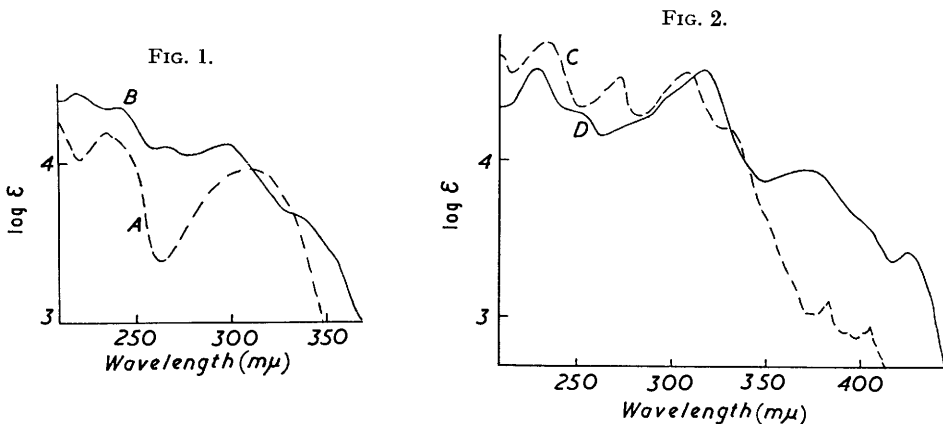


FIG. 1. Ultraviolet spectra of (A) potassium 1,2,7,8,9,10,11,14-octahydro-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylate [cf. (IV; R = R' = H)] [λ_{\max} . 263, 305 $m\mu$ (ϵ 39,100, 13,500)] and (B) potassium 1',1'',4',4''-tetraethoxy-1,2,7,8,9,10,11,14-octahydro-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylate [cf. (IV; R = H, R' = OEt)] [λ_{\max} . 221, 241, 265, 295 $m\mu$ (ϵ 27,800, 23,300, 12,700, 13,000)], both in water.

FIG. 2. Ultraviolet spectra of (C) potassium 3,4:5,6-dibenzophenanthrene-9,10-dicarboxylate [cf. (I; R = R' = H)] [λ_{\max} . 235, 272, 310, 328, 382, 405 $m\mu$ (ϵ 56,000, 32,700, 34,200, 15,800, 1300, 890)] and (D) potassium 1',1'',4',4''-tetraethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylate [cf. (I; R = H, R' = OEt)] [λ_{\max} . 229, 318, 370, 424 $m\mu$ (ϵ 37,100, 37,100, 8620, 2630)], both in water.

maleic anhydride adducts which were separated into their components. In order that they might be distinguished the symmetrical products were prepared from the individual tetralones. The unsymmetrically substituted adducts were thus recognisable. All these various adducts were dehydrogenated to the corresponding dibenzophenanthrene anhydrides for comparison of their properties. The two unsymmetrically substituted anhydrides in question were found to be distinct substances of widely differing m. p. Attempts at interconversion *via* the salts of the corresponding acids and by heat were ineffective. Hence structure (IX) is inapplicable.

One other alternative had to be examined before accepting the highly strained structure (V), namely, incomplete dehydrogenation of the adduct (IV). That a high degree of

dehydrogenation does take place was shown by carbon-hydrogen analysis and the profound change in colour, but neither of these facts would exclude the possibility of incomplete dehydrogenation to such a structure as (XI), which would undoubtedly be a highly coloured compound. Flexibility around $C_{(12)}$ and $C_{(13)}$ would allow sufficient folding to accommodate the alkoxyl groups R' and R'' without much strain. There would probably be insufficient rigidity for optical resolution. Such a structure was, however, excluded by the resistance of the substance to hydrogenation in the presence of a palladium catalyst at room temperature and pressures of hydrogen up to 65 atm.

The ultraviolet absorption spectrum of the adduct (IV; $R = R' = R'' = R''' = OEt$) in the form of the potassium salt of the corresponding acid in aqueous solution shows only a vague resemblance to that of the unsubstituted analogue (Fig. 1). The bands are less well-defined. This indicates that the substituents in the interfering positions cause a large departure from uniplanarity. The potassium salt of the dehydrogenated acid (I; $R = H, R' = OEt$) shows displacement of some of the bands to the red (Fig. 2). The general form of the curve resembles that of the unsubstituted acid (V; $R = R' = H$). This offers much support for the fully dehydrogenated structure (I).

EXPERIMENTAL

Conversion of Tetralones into Tetrahydrobinaphthyls (II \rightarrow III).—The method was essentially that already described.¹ Thus 7-methoxy-1-tetralone (35 g.) gave 3,3',4,4'-tetrahydro-7,7'-dimethoxy-1,1'-binaphthyl (21.5 g.), plates (from acetic acid), m. p. 154—155° (Found: C, 83.1; H, 7.0. $C_{22}H_{22}O_2$ requires C, 83.0; H, 7.0%). 5,8-Dimethoxy-1-tetralone (5 g.) gave 3,3',4,4'-tetrahydro-5,5',8,8'-tetramethoxy-1,1'-binaphthyl (2.5 g.), plates or needles (from acetic acid), m. p. 245—246° (Found: C, 75.8; H, 6.9. $C_{24}H_{26}O_4$ requires C, 76.2; H, 6.9%). 5,8-Diethoxy-1-tetralone (20 g.) gave 5,5',8,8'-tetraethoxy-3,3',4,4'-tetrahydro-1,1'-binaphthyl (8 g.), needles (from benzene), m. p. 212° (Found: C, 77.4; H, 8.0. $C_{28}H_{34}O_4$ requires C, 77.4; H, 7.9%). 8-Ethoxy-5-methoxy-1-tetralone (10 g.) gave 8,8'-diethoxy-3,3',4,4'-tetrahydro-5,5'-dimethoxy-1,1'-binaphthyl (5.1 g.), plates (from acetic acid), m. p. 194—195° (Found: C, 76.9; H, 7.7. $C_{26}H_{30}O_4$ requires C, 76.8; H, 7.4%). 5-Ethoxy-8-methoxy-1-tetralone (10 g.) gave 5,5'-diethoxy-3,3',4,4'-tetrahydro-8,8'-dimethoxy-1,1'-binaphthyl (5 g.), plates (from acetic acid), m. p. 224—225° (Found: C, 77.2; H, 7.8%). A mixture of 5,8-dimethoxy-1-tetralone and 5,8-diethoxy-1-tetralone gave mixed dienes which could not be separated by fractional crystallisation or chromatography. A mixture of 5-ethoxy-8-methoxy-1-tetralone and 8-ethoxy-5-methoxy-1-tetralone gave mixed dienes from which was separated by crystallisation from acetic acid on one occasion 5,8'-diethoxy-3,3',4,4'-tetrahydro-5',8'-dimethoxy-1,1'-binaphthyl, plates, m. p. 211—212° (Found: C, 76.5; H, 7.2%).

Maleic Anhydride Adducts from Tetrahydrobinaphthyls (III \rightarrow IV).—The procedure was as described.¹ 3,3',4,4'-Tetrahydro-7,7'-dimethoxy-1,1'-binaphthyl (20 g.) gave 1,2,7,8,9,10,11,14-octahydro-2'',3'-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (18 g.), recrystallised (from acetic acid), m. p. 182° (Found: C, 74.8; H, 5.9. $C_{26}H_{24}O_5$ requires C, 75.0; H, 5.8%). 3,3',4,4'-Tetrahydro-5,5',8,8'-tetramethoxy-1,1'-binaphthyl (4 g.) gave 1,2,7,8,9,10,11,14-octahydro-1'',4',4''-tetramethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (2.7 g.), orange yellow plates (from acetic acid), m. p. 310° (Found: C, 70.5; H, 6.0. $C_{28}H_{28}O_7$ requires C, 70.6; H, 5.9%). 5,5',8,8'-Tetraethoxy-3,3',4,4'-tetrahydro-1,1'-binaphthyl (8.5 g.) gave 1'',4',4''-tetraethoxy-1,2,7,8,9,10,11,14-octahydro-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (6.5 g.), yellow plates (from acetic anhydride), m. p. 274° (Found: C, 72.7; H, 7.1. $C_{32}H_{36}O_7$ requires C, 72.2; H, 6.8%). 5,5'-Diethoxy-3,3',4,4'-tetrahydro-8,8'-dimethoxy-1,1'-binaphthyl (4 g.) gave 1'',4''-diethoxy-1,2,7,8,9,10,11,14-octahydro-1'',4'-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (1.8 g.), yellow needles (from acetic acid), m. p. 252° (Found: C, 71.5; H, 6.4. $C_{30}H_{32}O_7$ requires C, 71.4; H, 6.4%). 8,8'-Diethoxy-3,3',4,4'-tetrahydro-5,5'-dimethoxy-1,1'-binaphthyl (4 g.) gave 1'',4'-diethoxy-1,2,7,8,9,10,11,14-octahydro-1'',4''-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (2.1 g.), yellow needles (from acetic acid), m. p. 284° (Found: C,

71.4; H, 6.4%). The inseparable mixture of dienes (3.7 g.) from 5,8-dimethoxy-1-tetralone and 5,8-diethoxy-1-tetralone gave a mixture of adducts separated by fractional crystallisation from acetic acid into two substances of m. p.s 311—313° and 256.5° severally. The first did not depress the m. p. of the tetramethoxy-adduct. The second differed from the tetraethoxy-adduct and was therefore 1',4'-diethoxy-1,2,7,8,9,10,11,14-octahydro-1'',4''-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (0.55 g.), pale yellow needles (Found: C, 71.3; H, 6.7%). The mixture of dienes (4 g.) from 5-ethoxy-8- and 8-ethoxy-5-methoxy-1-tetralone gave a mixture of adducts from which was separated by fractional crystallisation from acetic acid 1',1''-diethoxy-1,2,7,8,9,10,11,14-octahydro-4',4''-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (0.7 g.), orange-yellow needles, m. p. 305—306° (Found: C, 71.1; H, 6.7%).

Dehydrogenation of Adducts (IV).—(a) *By bromine.* The above-mentioned dimethoxy-adduct (5 g.) in chloroform was treated slowly with bromine (4 g.) in acetic acid. The solution soon deposited yellow plates (4.7 g.), m. p. 285° (Found: C, 54.7; H, 3.2; Br, 26.9. $C_{26}H_{18}O_5Br_2$ requires C, 54.8; H, 3.2; Br, 28.0%). Simultaneous bromination and dehydrogenation had taken place and the compound produced was 2',3''-dibromo-1,2,7,8-tetrahydro-2'',3'-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride, its state of oxidation being confirmed also by its yellow colour.

(b) *By lead tetra-acetate.* The dimethoxy-adduct (3 g.) in acetic acid (15 ml.) and acetic anhydride (15 ml.) was heated with lead tetra-acetate (7 g.) at 100° for 1 hr. On cooling, yellow needles of a substance separated, having m. p. 235° (from chloroform) (Found: C, 75.1; H, 5.0. $C_{26}H_{20}O_5$ requires C, 75.7; H, 4.9%). The diethoxy-adduct gave a similar substance, orange-red needles, m. p. 248° (Found: C, 72.0; H, 5.8%; equiv., 316. $C_{32}H_{32}O_7$ requires C, 72.7; H, 6.1%; equiv., 264). Since these analyses are not in good agreement and since the compounds gave products of indefinite composition on further dehydrogenation it was considered that they had become acetylated or acetoxylated.

(c) *By palladium.* The dimethoxy-adduct (4 g.) was heated with palladium-charcoal (0.4 g.) at 340—350° for 10 min., giving 2'',3'-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (1.6 g.) as orange-red needles (from acetic anhydride), m. p. 269—270° (Found: C, 76.1; H, 4.0. $C_{26}H_{18}O_5$ requires C, 76.5; H, 4.0%). The tetramethoxy-adduct (1 g.) with palladium charcoal (0.1 g.) for 20 min. at 350° gave crimson crystals, m. p. 292°, of variable composition. Products from the tetraethoxy-adduct were also unsatisfactory; e.g., heating this adduct (0.9 g.) with palladium-charcoal (0.15 g.) at 300° for 4 hr. produced neutral orange-red plates (0.3 g.), m. p. 267—268°, almost certainly 4,9-diethoxy-2,3,10,11-tetrahydro-1,12-benzoperylene (Found: C, 85.0; H, 6.6. $C_{26}H_{24}O_2$ requires C, 84.8; H, 6.6%).

(d) *By palladium and sulphur.* The dimethoxy-adduct was dehydrogenated successfully with sulphur and with selenium but several hours' heating was required. The tetramethoxy-adduct did not give a pure product with sulphur. A mixture of sulphur and palladium-charcoal brought about rapid dehydrogenation at a lower temperature to a pure product. A mixture of the tetramethoxy-adduct (0.5 g.), palladium-charcoal (0.05 g.), and sulphur (0.15 g.) was heated at 300° for 5 min. A chloroform extract of the cooled mixture gave a residue affording, on recrystallisation from acetic anhydride, 1',1'',4',4''-tetramethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (0.22 g.), very deep red or crimson prisms, m. p. 323.5° (Found: C, 71.2; H, 4.1%; equiv., 241. $C_{28}H_{20}O_7$ requires C, 71.8; H, 4.3%; equiv., 243). Slight demethylation occasionally took place and was corrected by treatment of the product with dimethyl sulphate. Similar dehydrogenation of the tetraethoxy-adduct (1.6 g.), but for 12 min., gave 1',1'',4',4''-tetraethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (1.1 g.), maroon needles (from acetic anhydride), m. p. 295—296° (Found: C, 73.4; H, 5.5. $C_{32}H_{28}O_7$ requires C, 73.3; H, 5.4%). Dehydrogenation (7 min.) of 1',4'-diethoxy-1,2,7,8,9,10,11,14-octahydro-1'',4''-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride gave 1',4'-diethoxy-1'',4''-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride, garnet plates, m. p. 272—273°, in good yield (Found: C, 72.1; H, 5.2. $C_{30}H_{24}O_7$ requires C, 72.6; H, 4.9%). This substance did not change in 4 hr. at 280°. It was regenerated unchanged from the salts of the corresponding acid. The 1',4''-diethoxy-1'',4'-dimethoxy-adduct gave 1',4''-diethoxy-1'',4'-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (good yield), deep red plates, m. p. 257.5° (Found: C, 72.5; H, 5.0%). The 1'',4'-diethoxy-1',4''-dimethoxy-adduct gave 1'',4'-diethoxy-1',4''-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride, deep red plates, m. p. 293° (Found: C, 72.4; H, 5.2%).

The 1',1''-diethoxy-4',4''-dimethoxy-adduct gave 1',1''-diethoxy-4',4''-dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride, deep red plates, m. p. 308° (Found: C, 72.7; H, 5.0%). This substance did not change in 4 hr. at 280°. It was regenerated unchanged from the salts of the corresponding acid.

Distillations with Zinc Dust.—3,3',4,4'-Tetrahydro-5,5',8,8'-tetramethoxy-1,1'-binaphthyl (1 g.) was dehydrogenated (5 min. at 280°) with palladium-charcoal and sulphur as above, to give 5,5',8,8'-tetramethoxy-1,1'-binaphthyl (0.89 g.), dull yellow plates (from acetic acid), m. p. 131.5° (Found: C, 76.5; H, 5.8. $C_{24}H_{22}O_4$ requires C, 77.0; H, 5.9%). This compound, or better, the crude material obtained on demethylating it by boiling hydriodic acid (*d* 1.7) for 4 hr., was mixed with excess of zinc dust and heated. A good yield of sublimate was obtained, as golden-yellow plates, m. p. 274°, shown to be perylene by its ultraviolet absorption spectrum and colour reactions.

1',1'',4',4''-Tetramethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic anhydride (1 g.) in acetic anhydride (20 ml.) was refluxed for 6 hr. with hydriodic acid (*d* 1.7; 40 ml.). On cooling and dilution, a dark precipitate was obtained which was extracted with sodium hydroxide solution, and the filtrate was acidified. This precipitate was heated with zinc dust in excess, giving a sublimate (0.12 g.) of yellow plates, m. p. 264°; after recrystallisation twice from acetic acid, these had m. p. 271°. The ultraviolet absorption showed them to be 1,12-benzoperylene.

Optical Resolution of 2',3'-Dimethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic Acid.—The potassium salt of this acid was prepared by refluxing the corresponding anhydride with 10% potassium hydroxide solution. An aqueous solution of the salt was acidified with hydrochloric acid, and the acid (1.1 g.) filtered off, dried and suspended in boiling ethanol (20 ml.) to which morphine (0.7 g.) was added. Refluxing was continued until a clear solution was obtained. Filtration and cooling produced two crops of morphine salt, and a third was obtained by evaporation of the mother-liquor. The first fraction of *morphine salt*, had m. p. 230°, $[\alpha]_D^{20} + 392^\circ$ (in $CHCl_3$) (Found: N, 2.0. $C_{43}H_{37}O_9N$ requires N, 1.7%). Decomposition gave the active *acid*, m. p. 182°, $[\alpha]_D^{20} + 677^\circ$ (in acetone) (Found: C, 74.4; H, 3.8. $C_{26}H_{18}O_8$ requires C, 73.2; H, 4.3%). The acid had reverted partially to the anhydride by the time it was analysed. The third fraction of morphine salt, m. p. 212—214°, had $[\alpha]_D^{20} - 357^\circ$ (in EtOH). Decomposition gave the active *acid*, $[\alpha]_D^{20} - 640^\circ$ (in acetone). The rotations of the acetone solutions of both forms of the acid decreased to zero in 4 days at room temperature.

Attempted Resolution of 1',1'',4',4''-Tetramethoxy-3,4:5,6-dibenzophenanthrene-9,10-dicarboxylic Acid.—The acid, obtained from the anhydride as above, had m. p. 220—245°. It reverted completely to the anhydride in 2 days at room temperature. The morphine salt was non-crystalline and very soluble in all solvents tried. Decomposition gave inactive acid. Similar results were obtained by using brucine, cinchonine, cinchonidine, ephedrine, and 1-phenylethylamine. The strychnine salt crystallised well from ethanol but did not give active acid on decomposition.