*Anal.* Calcd. for $C_{22}H_{31}NO_3$: C, 73.90; H, 8.74; N, 3.92. Found: C, 73.9; H, 8.7; N, 4.2.

**Acknowledgment.**—The authors greatly appreciate the technical assistance given by Mrs. G. A. Snyder and the gas chromatographic work done by Mr. Horace Warrington of this institute. Further, they thank Mr. K. D. Fleischer and his associates for their analytical work and Dr. F. C. Nachod and his associates for the spectral data.

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# Tumor Inhibitors. X.[1] Photochemical Synthesis of Phenanthrenes. Synthesis of Aristolochic Acid and Related Compounds[2-4]

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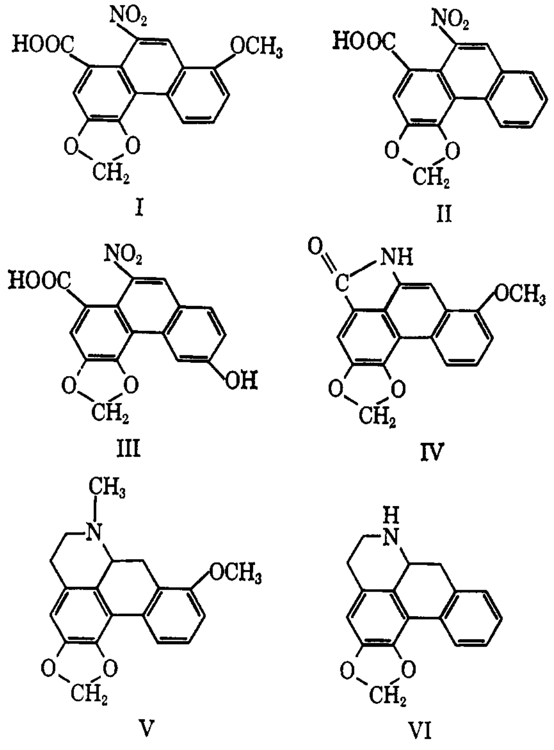
A new general synthesis of substituted phenanthrene derivatives, involving photocyclization of substituted 2-iodostilbenes, is presented herewith. The usefulness of this method for the synthesis of nitrophenanthrenes, not readily accessible by other approaches, is illustrated in an efficient synthesis of the naturally occurring tumor inhibitor, aristolochic acid, and several related analogs.

During the course of a search for tumor inhibitors from plant sources, Kupchan and Doskotch[6] found that *Aristolochia indica* L. possessed reproducible activity against the adenocarcinoma 755 test system. Aristolochic acid I (I) was characterized as the tumor-inhibitory principle. This acid was subsequently tested in mice for carcinogenic activity and was found to produce papillomas when applied topically with croton oil.[7] The structure elucidation of aristolochic acid is credited mainly to Pailer and co-workers.[8] The family *Aristolochiaceae* comprises approximately 180 species. Many of these have played important roles in folk medicine as wound healers, snake bite remedies, fever cures, and as the name itself implies, in childbirth.

Few naturally occurring nitro-containing compounds are known, and these few were discovered relatively recently. The first and, perhaps, best known of this group, chloramphenicol, was fully characterized in 1949.[9] Soon after this discovery, two glycosides, hiptagin and karakin, were isolated and characterized as derivatives of $\beta$-nitropropionic acid.[10] Various species of the genus *Aristolochia* have been found to yield substituted nitrophenanthrene derivatives: aristolochic acid I (I), aristolochic acid II (II), aristolochic acid C (III), aristolactam (IV), and three compounds of unknown structure, aristolochic acid B, debilic acid, and aristo-red.[11] It has been postulated that aporphine alkaloids such as stephanine (V) and anonaine (VI) (Chart I) may be biogenetically precursorial to the aforementioned compounds.[11]

CHART I



I II III IV V VI

Kharasch has described a synthesis of polyphenyl compounds by photolysis of the corresponding iodoaromatic compounds in benzene using a cold-cathode, low-pressure mercury arc with Vycor glass housing.[12,13] Photolysis in cyclohexane, methanol, or ethanol causes reductive deiodination, and the reaction appears to have wide applicability. Photolysis in other aromatic solvents such as molten naphthalene and biphenyl gives the isomeric 1- and 2-phenylnaphthalenes and isomeric terphenyls in the ratio expected for homolytic phenylation.

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[1] Part IX: S. M. Kupchan and H. C. Wormser, *J. Org. Chem.*, **30**, 3933 (1965).

[2] The investigation which forms the subject of this paper was first outlined in part in a preliminary communication: S. M. Kupchan and H. C. Wormser, *Tetrahedron Letters*, 359 (1965).

[3] This investigation was supported in part by research grants from the National Cancer Institute (CA-04500) and the American Cancer Society (T-275).

[4] Abstracted from a part of the dissertation submitted by H. C. Wormser to the University of Wisconsin Graduate School, June 1965, in partial fulfillment of the requirements of the Ph.D degree.

[5] American Foundation for Pharmaceutical Education Fellow, 1961–1963; National Institutes of Health Predoctoral Fellow, 1963–1965.

[6] S. M. Kupchan and R. W. Doskotch, *J. Med. Pharm. Chem.*, **5**, 657 (1962).

[7] Appreciation is expressed to Professor R. K. Boutwell of the McArdle Memorial Laboratory at the University of Wisconsin for the study on the carcinogenic activity of aristolochic acid I.

[8] M. Pailer, L. Belohlav, and E. Simonisch, *Monatsh.*, **87**, 249 (1956).

[9] M. C. Rebstock, H. M. Crooks, Jr., J. Controulis, and Q. R. Bartz, *J. Am. Chem. Soc.*, **71**, 2458 (1949).

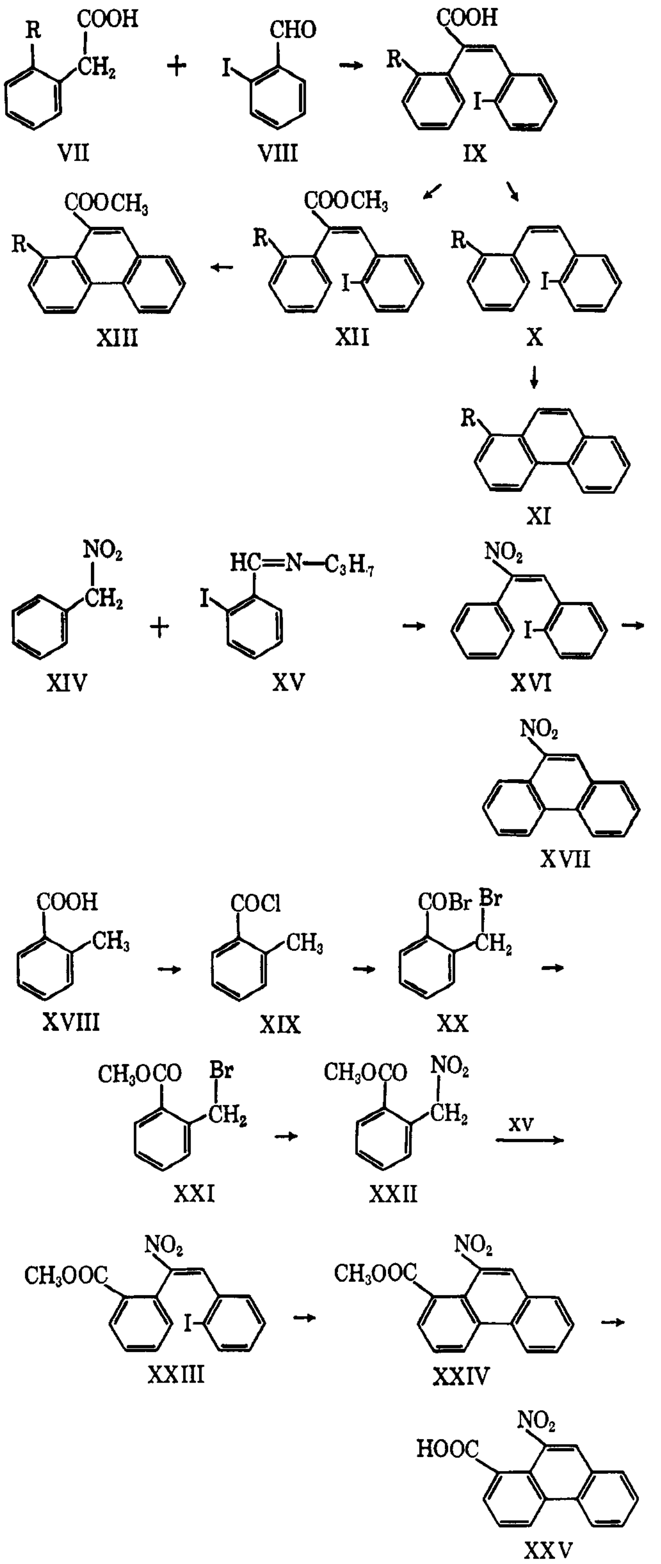
[10] L. Carter and W. J. McChesney, *Nature*, **164**, 575 (1949).

[11] H. G. Boit, "Ergebnisse der Alkaloid-Chemie Bis 1960," Akademie-Verlag G.m.b.H., Berlin, 1961, p. 270.

[12] W. Wolf and N. Kharasch, *J. Org. Chem.*, **26**, 283 (1961).

[13] N. Kharasch and L. Göttlich, *Angew. Chem.*, **74**, 651 (1962).

Chart II

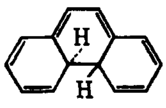


In this study, the photolysis of iodoaromatic compounds was used in an *intramolecular* reaction to effect photocyclization. Thus, 2-iodo-*cis*-stilbene (X, R = H), prepared by the copper chromite decarboxylation of 2′-iodo-*cis*-stilbene-α-carboxylic acid (IX, R = H), which in turn had been synthesized by a Perkin condensation of phenylacetic acid (VII, R = H) and *o*-iodobenzaldehyde (VIII) in acetic anhydride, was chosen as the simplest model phenanthrene precursor for the new reaction (see Chart II). Photolysis of X, R = H, in cyclohexane for 3 hr. at room temperature, with a Nester–Faust NFUV-300 ultraviolet source, afforded phenanthrene (XI, R = H), in 90% yield. The progress of the reaction was followed by ultraviolet spectral analysis after appropriate time intervals. Similarly, 2-methyl-2′-iodo-*cis*-stilbene (X, R = $CH_3$), photolyzed for 4 hr., afforded XI, R = $CH_3$, in 96% yield, melting point undepressed upon admixture with an authentic sample prepared as described by Pschorr.[14] The stilbene X, R = $CH_3$, was prepared analogously to 2-iodo-*cis*-stilbene, by the condensation of 2-methylphenylacetic acid (VII, R = $CH_3$) with the aldehyde VIII, and subsequent decarboxylation of the resultant acid (IX, R = $CH_3$) in quinoline with copper chromite catalyst.

The methyl ester of 2-iodo-*cis*-stilbene-α-carboxylic acid (XII, R = H) afforded, in 71% yield, 9-phenanthroic acid methyl ester (XIII, R = H). The methyl ester of 2-methyl-2′-iodo-*cis*-stilbene-α-carboxylic acid (XII, R = $CH_3$) gave a 62% yield of 1-methyl-10-phenanthroic acid methyl ester (XIII, R = $CH_3$), melting point undepressed upon admixture with material prepared by diazomethane methylation of the corresponding acid.[14]

α-Nitro-2′-iodo-*cis*-stilbene (XVI) was synthesized by the condensation of phenylnitromethane (XIV) with the *n*-propylidene base of *o*-iodobenzaldehyde (XV) according to the general method of Robertson.[15] Photolysis of the stilbene XVI gave a 40% yield of 9-nitrophenanthrene (XVII). Analogously, 2-carbomethoxy-2′-iodo-α-nitro-*cis*-stilbene (XXIII), prepared as shown on Chart II, when photolyzed afforded, in 50% yield, the methyl ester of 10-nitro-1-phenanthroic acid (XXIV). Chemical evidence for the structure XXIV was obtained by ethanolic potassium hydroxide hydrolysis of the ester to the free acid XXV and copper–quinoline decarboxylation to the known 9-nitrophenanthrene (XVII). In addition, the acid XXV was characterized by direct comparison with a sample prepared by an alternate route.[1]

Irradiation with ultraviolet light of solutions containing *cis*-stilbenes in the presence of a suitable oxidant such as molecular oxygen or iodine has been demonstrated to lead to formation of phenanthrene derivatives.[16] Evidence which strongly indicates that the latter reaction proceeds *via* the dihydrophenanthrene XXVI has recently been presented.[17,18]



XXVI

It is highly improbable that the photocyclization of 2-iodostilbenes proceeds *via* a similar intermediate. Photolysis of 2-carbomethoxy-α-nitro-*cis*-stilbene (XXVII), in the presence of added iodine or dissolved molecular oxygen, failed to yield any of the corresponding

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(14) R. Pschorr, *Ber.*, **39**, 3106 (1906).

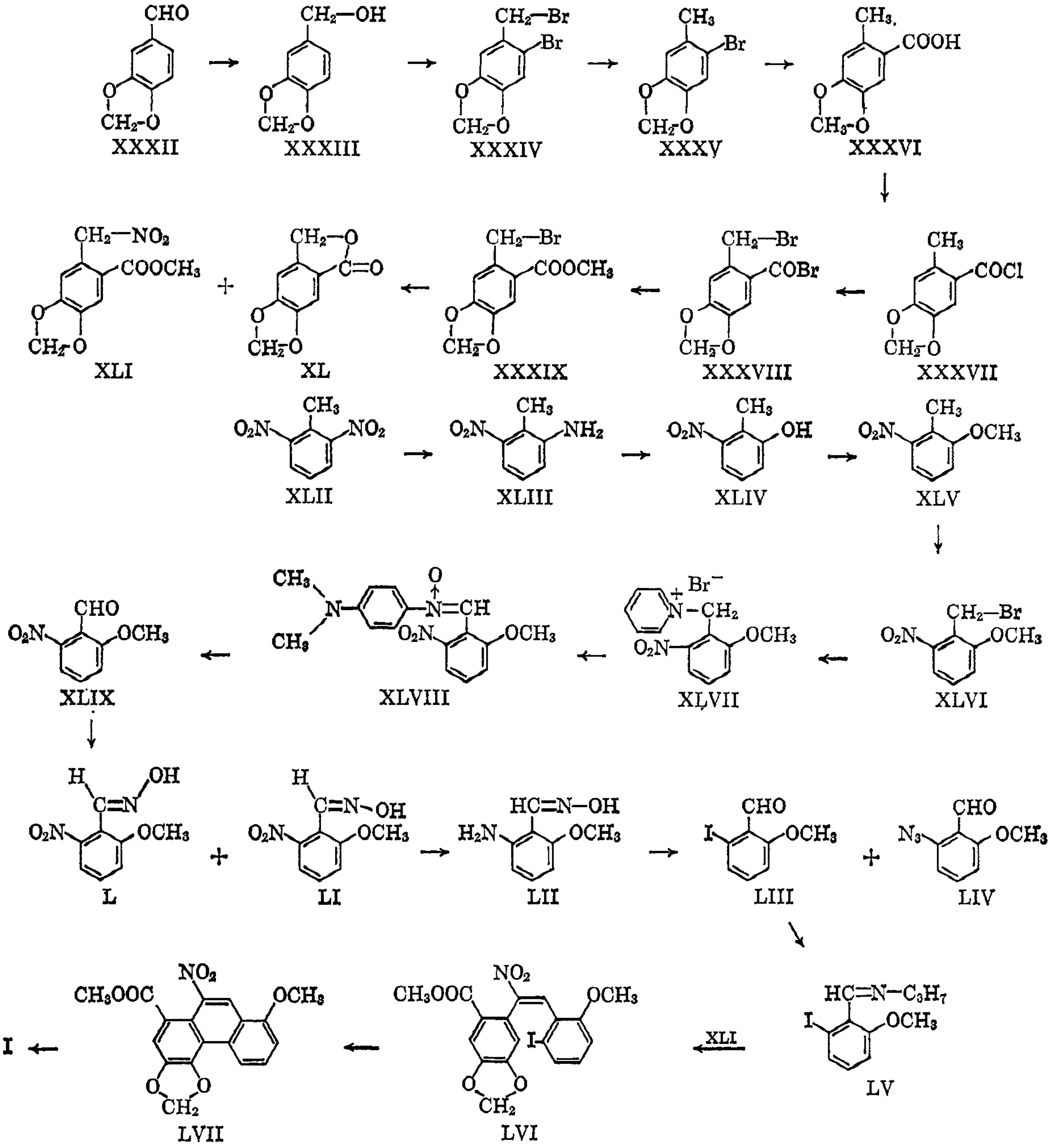
(15) D. N. Robertson, *J. Org. Chem.*, **25**, 47 (1960).

(16) F. B. Mallory, C. S. Wood, and J. T. Gordon, *J. Am. Chem. Soc.*, **86**, 3094 (1964), and earlier references cited there.

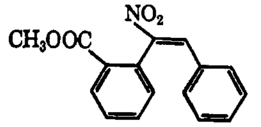
(17) W. M. Moore, D. D. Morgan, and F. R. Stermitz, *ibid.*, **85**, 829 (1963).

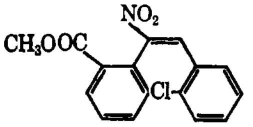
(18) G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Cowan, R. C. Counsell, V. Vogt, and C. Dalton, *ibid.*, **86**, 3197 (1964).

Chart III



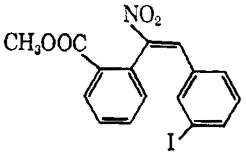
phenanthrene. Failure of stilbenes having nitro substituents to undergo photoconversion to the corresponding phenanthrenes has been noted previously.[16] In the present work, 2-carbomethoxy-2′-chloro-α-nitro-*cis*-stilbene (XXVIII), when subjected to irradiation


XXVII

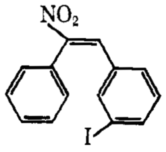

XXVIII

at 2537 Å., failed to undergo cyclization, and the latter observation militates strongly against the intermediacy of an unorthodox dihydrophenanthrene such as XXVI in the photocyclization of 2-iodostilbenes. A recent electron spin resonance study of the photolysis of iodobenzene at 77°K. yielded results which support the occurrence of the "free" phenyl radical intermediate in the photoconversion of iodobenzene to biphenyl.[19] A singlet 16-gauss broad e.s.r. spectrum was observed. It is suggested that the photocyclization of 2-iodostilbenes may likewise proceed *via* a free-radical pathway. An experiment to provide resonance evidence for such a species was conducted on 2-iodo-*cis*-stilbene (X, R = H). In our case also a weak, broad, singlet resonance signal was obtained. A brief temperature study revealed no fine structure in the signal, so that the true nature of the phenyl radical is still obscure. In this study the photolysis was run outside the cavity at 77°K. in a 3-methylpentane-glass matrix.

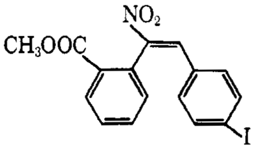
Experiments were also devised to evaluate the integrity of the free radical produced by photolysis of the carbon–iodine bond. If free-radical rearrangements occurred, cleavage of 2-, 3-, or 4-iodo-substituted stilbenes might have yielded a common product. Photolyses of 2-carbomethoxy-3′-iodo-α-nitro-*cis*-stilbene (XXIX), 3′-iodo-α-nitro-*cis*-stilbene (XXX), and 2-carbomethoxy-4′-iodo-α-nitro-*cis*-stilbene (XXXI), afforded no phenanthrene product, as shown by thin layer chromatography on silica gel and ultraviolet spectral analysis.



XXIX



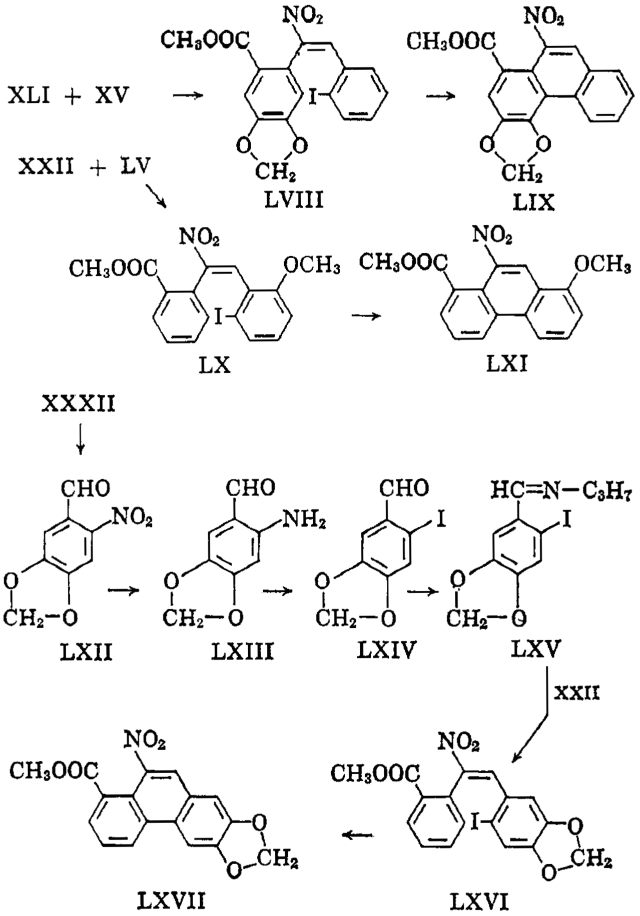
XXX



XXXI

Piperonal (XXXII) provided a suitable basic skeleton on which to build ring A of both aristolochic acid I and aristolochic acid II (see Chart III). In the present investigation XXXII was reduced to the desired piperonyl alcohol, in quantitative yield, with lithium aluminum hydride in anhydrous ether.[20] Bromination of the alcohol XXXIII was effected by the use of bromine in glacial acetic acid[21] and afforded 6-bromopiperonyl bromide (XXXIV) in 68% yield. The benzyl bromide was hydrogenolyzed to the corresponding 2-bromo-4,5-methylenedioxytoluene (XXXV) by the action of lithium aluminum hydride in refluxing tetrahydrofuran (77% yield). Using the *n*-butyllithium carbonation method, the *o*-toluic acid XXXVI was prepared in 41% yield. Intermediates XXXVII and XXXVIII were not isolated from their respective reaction mixtures. Compound XXXVI was converted to the acid chloride XXXVII by the action of oxalyl chloride in benzene; this in turn was side-chain brominated to the dihalide XXXVIII. Addition of anhydrous methanol to the cooled reaction mixture afforded the crystalline ester XXXIX in 46% over-all yield. Treatment of this compound with silver nitrate in anhydrous ether afforded two products separated by chromatography on silica gel. The compound with the higher $R_f$ value was obtained in 45% yield and its infrared spectrum was in agreement with structure XLI. The compound with the lower $R_f$ value, XL, was characterized as 4,5-methylenedioxyphthalide by direct comparison with material prepared by the method of Stevens and Robertson.[22,23]

CHART IV



Synthesis of the ring-C precursor of aristolochic acid I is shown on Chart III and involved the sequence XLII → LV. The readily available 2-nitro-6-methoxytoluene (XLV) was oxidized to the nitroaldehyde XLIX by the Krönhke reaction.[24] Reduction of the nitroaldehyde XLIX to the amine LII and Sandmeyer conversion to the *o*-iodoaldehyde LIII were effected by the general method of Mayer.[25] It was found necessary to protect the aldehyde function by conversion to the oxime because of the extreme sensitivity of *o*-aminobenzaldehydes toward traces of mineral acids. Thin layer chromatography of the oxime showed the product to be a mixture of two closely related compounds, having similar $R_f$ values. These two compounds were characterized as isomeric oximes [*syn* or α (L) and *anti* or β (LI)] by elemental analysis and infrared evidence.[26] 2-Amino-6-methoxybenzaldoxime (LII) was obtained by alkaline ferrous hydroxide reduction of the mixture of nitro oximes. Only one geometrical form was obtained, in 68% yield. The desired *o*-iodobenzaldehyde LIII was prepared in 40% yield by a Sandmeyer-type reaction and was characterized as the 2,4-dinitrophenylhydrazone. The reaction mixture afforded a second product, characterized as 2-azido-6-methoxybenzaldehyde (LIV) on the basis of its elemental analysis and origin.[27] The condensation of XLI with the *n*-propylidene base LV was effected in glacial acetic acid, and a 64% yield of 2-carbomethoxy-4,5-methylenedioxy-2′-iodo-6′-methoxy-α-nitro-*cis*-stilbene (LVI) was obtained. Photolysis of this stilbene afforded, in 54% yield, aristolochic acid methyl ester (LVII), melting point undepressed upon admixture with an authentic sample.[6] The infrared spectrum (KBr) was superimposable upon that of the authentic sample.

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[19] R. B. Ingalls, W. Wolf, and N. Kharasch, Abstracts, 146th National Meeting of the American Chemical Society, Denver, Colo., Jan. 1964, p. 6D.

[20] E. Larsson, *Trans. Chalmers Univ. Technol., Gothenburg*, **94**, 15 (1950); *cf. Chem. Abstr.*, **45**, 1494 (1951).

[21] W. E. Barthel and B. H. Alexander, *J. Org. Chem.*, **23**, 1012 (1958).

[22] T. S. Stevens, *J. Chem. Soc.*, 178 (1927).

[23] T. S. Stevens and M. C. Robertson, *ibid.*, 2790 (1927).

[24] S. M. Kupchan and J. J. Merianos, unpublished results.

[25] F. Mayer, *Ber.*, **45**, 1105 (1912).

[26] A. Palm and H. Werbin, *Can. J. Chem.*, **31**, 1004 (1953).

[27] J. H. Boyer and F. C. Carter, *Chem. Rev.*, **54**, 1 (1954).

Similarly, photolysis of 2-carbomethoxy-4,5-methylenedioxy-2′-iodo-α-nitro-*cis*-stilbene (LVIII) yielded (26%) aristolochic acid II methyl ester (LIX) (Chart IV). Two additional nitrophenanthroic acid methyl esters were prepared as analogs of aristolochic acid I. Condensation of 2-carbomethoxyphenylnitromethane (XXII) with the *n*-propylidene base of 2-iodo-6-methoxybenzaldehyde (LV) afforded a 64% yield of 2-carbomethoxy-2′-iodo-6′-methoxy-α-nitro-*cis*-stilbene (LX). Photolysis in cyclohexane yielded (60%) 1-carbomethoxy-8-methoxy-10-nitrophenanthrene (LXI). Condensation of XXII with the *n*-propylidene base of 6-iodopiperonal (LXV) afforded a 32% yield of 2-carbomethoxy-2′-iodo-4′,5′-methylenedioxy-α-nitro-*cis*-stilbene (LXVI). Photolysis yielded 1-carbomethoxy-6,7-methylenedioxy-10-nitrophenanthrene (LXVII).

## Experimental Section[28]

***o*-Iodobenzaldehyde (VIII)** was prepared according to the method of Weitzenböck,[29] m.p. 37°, in 68% yield (lit.[29] m.p. 37°).

**2′-Iodo-*cis*-stilbene-α-carboxylic Acid (IX, R = H).**—In a three-necked, 200-ml., round-bottom flask, provided with a mechanical stirrer and water condenser, was placed a mixture of *o*-iodobenzaldehyde (VIII, 8.14 g., 0.0350 mole, m.p. 37°), phenylacetic acid (VII, R = H, 5.26 g., 0.040 mole, m.p. 77°), potassium carbonate (2.42 g., 0.016 mole), and acetic anhydride (15 ml.). The white creamy suspension was stirred and refluxed for 6 hr. during which time the mixture became clear. Water was added to the cloud point and a crystalline material separated on cooling (11.54 g.), m.p. 170–175°. Three recrystallizations from ethyl acetate afforded fine colorless needles (9.84 g., 80%), m.p. 179–180°, $\lambda_{\max}^{\mathrm{Nujol}}$ 5.99 μ.

**2-Iodo-*cis*-stilbene (X, R = H).**—Quinoline (20 ml.), in a 50-ml. round-bottom flask fitted with an air condenser, was heated to 225° in an oil bath. Black copper chromite catalyst (0.250 g.) was added at once and the temperature was raised to 230°. 2′-Iodo-*cis*-stilbene-α-carboxylic acid (IX, R = H, 2.0 g., 0.0056 mole, m.p. 179–180°) was added in small portions to the hot mixture. A strong evolution of $CO_2$ was observed. The reaction mixture was heated at 230° for an additional 30 min. After rapid cooling, the quinoline slurry was poured into 10% hydrochloric acid (250 ml.), and the undissolved black oil was extracted with chloroform. The chloroform extract was treated stepwise with 10% hydrochloric acid, saturated potassium carbonate solution, and water, and finally dried over magnesium sulfate. Evaporation of the solvent under reduced pressure afforded a brown oil (1.89 g.). Filtration over a silica gel column with Skellysolve B, followed by distillation under reduced pressure, afforded a colorless oil (1.51 g., 88%), b.p. 125–127° (0.5 mm.). Gas chromatography on an Apiezon L column (F & M Scientific Corp.) and thin layer chromatography on silica gel G showed the homogeneity of the product. The infrared spectrum showed the diagnostic peaks of 2-substituted stilbenes at 10.90 and 12.80 μ: $\lambda_{\max}^{\mathrm{EtOH}}$ 271.5 mμ (ε 16,900).

**Isomerization of 2-Iodo-*cis*-stilbene to the *trans* Isomer.**—A solution of 2-iodo-*cis*-stilbene (X, R = H) in nitrobenzene (5 ml.) containing a small crystal of iodine was refluxed for 1 hr. in an oil bath. The nitrobenzene was distilled under vacuum and the residue was purified by preparative t.l.c. on silica gel G (Skellysolve B as the eluent). The thick oil which was obtained (0.175 g.) was crystallized by the addition of a few drops of methanol (0.170 g., 85%), m.p. 51–54°. Recrystallization from methanol afforded shiny, colorless crystals (0.157 g.), m.p. 54–56° (lit.[30] m.p. 55–56°).

The infrared and ultraviolet spectra were in agreement with the *trans* structure: $\lambda_{\max}^{\mathrm{CHCl_3}}$ 10.41 μ (*trans*-stilbene), $\lambda_{\max}^{\mathrm{EtOH}}$ 297 mμ (ε 25,000).

**Photolysis of 2-Iodo-*cis*-stilbene. Phenanthrene (XI, R = H).**—In a three-necked flask (Nester–Faust Co.), fitted with a Teflon magnetic stirrer and a Nester–Faust NFUV-300 ultraviolet light source, was placed 2-iodo-*cis*-stilbene [X, R = H, 0.100 g., 0.00033 mole, b.p. 125–127° (0.5 mm.)] in purified cyclohexane (475 ml.). The progress of the reaction was followed by ultraviolet spectral analysis after appropriate time intervals (appearance of a high-intensity band at 251.5 mμ). Reaction time was 3 hr. Evaporation of the solvent with the formed iodine under reduced pressure afforded a brown oil (0.067 g.). Preparative thin layer chromatography on silica gel $HF_{254+366}$ (Skellysolve B elution) afforded shiny plates (0.052 g., 90%), m.p. 95–97° (lit.[31] m.p. 97°).

**2-Methyl-2′-iodo-*cis*-stilbene-α-carboxylic Acid (IX, R = $CH_3$).**—The same procedure and identical quantities of reactants [in this case, VII (R = $CH_3$) and VIII] were used for the synthesis of compound IX, R = $CH_3$, as described for the synthesis of IX, R = H. The tan product which was obtained (10.84 g., m.p. 152–162°) was sublimed at 140° (0.05 mm.). The compound was recrystallized twice from aqueous ethanol, affording a colorless crystalline product (8.05 g., 63%), m.p. 162–165°.

*Anal.* Calcd. for $C_{16}H_{13}IO_2$: C, 52.77; H, 3.60. Found: C, 53.21; H, 3.48.

**2-Methyl-2′-iodo-*cis*-stilbene (X, R = $CH_3$).**—The same procedure and identical quantities of reagents were used for decarboxylation of IX, R = $CH_3$, as described for the synthesis of X, R = H. Vacuum distillation of the oil afforded 1.42 g. (79%) of product, b.p. 104–105° (0.07 mm.). V.p.c. analysis showed the product to be homogeneous: $\lambda_{\max}^{\mathrm{EtOH}}$ 265 mμ (ε 23,400).

**Photolysis of 2-Methyl-2′-iodo-*cis*-stilbene. 1-Methylphenanthrene (XI, R = $CH_3$).**—The photolysis reaction was run on 2-methyl-2′-iodo-*cis*-stilbene [X, R = $CH_3$, 0.100 g., 0.00031 mole, b.p. 104–105° (0.07 mm.)] in cyclohexane (475 ml.) for 4 hr. Work-up and preparative t.l.c. on silica gel G (Skellysolve B) afforded 1-methylphenanthrene (0.062 g.), m.p. 118–120°. Recrystallization from aqueous ethanol afforded shiny plates (0.061 g., 96%), m.p. 122–123° (lit.[14] m.p. 123°), undepressed upon admixture with a sample prepared according to the procedure of Pschorr.[14]

**Methyl Ester of 2′-Iodo-*cis*-stilbene-α-carboxylic Acid (XII, R = H).**—To a 100-ml. erlenmeyer flask were added IX, R = H (0.250 g., 0.00071 mole, m.p. 179–180°), and anhydrous ether (50 ml.). To this solution was added an excess of diazomethane in ether, and the resulting yellow solution was allowed to stand at room temperature for 3 hr. Evaporation of the ether and unreacted diazomethane afforded a yellow viscous oil (0.261 g.). Chromatography on silica gel (Skellysolve B elution) gave a colorless solid (0.242 g.). Recrystallization of this material from Skellysolve B afforded colorless crystals (0.232 g., 89%), m.p. 98–100°, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.82 μ, $\lambda_{\max}^{\mathrm{EtOH}}$ 286 mμ (ε 11,000).

*Anal.* Calcd. for $C_{16}H_{13}IO_2$: C, 52.77; H, 3.59. Found: C, 52.59; H, 3.44.

**Methyl Ester of 9-Phenanthroic Acid (XIII, R = H).**—The photolysis reaction was effected on 2′-iodo-*cis*-stilbene-α-carboxylic acid methyl ester (XII, R = H, 0.100 g., 0.00027 mole, m.p. 98–100°) in cyclohexane (475 ml.) for 4 hr. The usual work-up afforded a crystalline product (0.050 g., m.p. 110–115°). Recrystallization from ethanol gave shiny colorless crystals (0.046 g., 71%), m.p. 118–119° (lit.[32] m.p. 116°).

**Methyl Ester of 2-Methyl-2′-iodo-*cis*-stilbene-α-carboxylic Acid (XII, R = $CH_3$).**—Diazomethane methylation of IX was effected similarly and on the same quantity of acid as used for the synthesis of XII, R = H. Work-up and recrystallization were also identical. A colorless crystalline product was obtained

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(28) Melting points were determined on a Fisher-Johns melting point stage which had been calibrated with standard samples. Ultraviolet absorption spectra were determined in 95% ethanol on a Beckman (Model DK2A) *recording spectrophotometer* and a Cary (Model II-MS) recording spectrophotometer. Infrared absorption spectra were recorded in chloroform (unless otherwise specified) on a Beckman (Model 5A) double-beam infrared recording spectrophotometer. Microanalyses were by J. F. Alicino, Metuchen, N. J., and Spang Microanalytical Laboratory, Ann Arbor, Mich. N.m.r. spectra were recorded on a Varian Associates recording spectrophotometer (A60) at 60 Mc./sec. in deuterated chloroform, with tetramethylsilane as internal standard. Chemical shifts recorded in τ values (p.p.m.) [G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958)]. Skellysolve B refers to petroleum ether, fraction boiling at 60–68°. Electron paramagnetic resonance spectra were recorded on a Varian Associates 4500 basic spectrometer with 100-kc. modulation. Gas chromatography analyses were performed on an F & M laboratory chromatograph, Model 700. Thin layer chromatography (t.l.c.) was carried out with silica gel G and silica gel $HF_{254+366}$ (Brinkmann Instruments).

(29) R. Weitzenböck, *Monatsh.*, **34**, 193 (1913).

(30) G. Drefahl and G. Langbein, *Ber.*, **90**, 145 (1957).

(31) W. G. Brown and B. Bluestein, *J. Am. Chem. Soc.*, **62**, 3256 (1940).

(32) E. Mosettig and J. van de Kamp, *ibid.*, **52**, 3704 (1930).

(0.240 g., 93%): m.p. 92–94°, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.82 μ, $\lambda_{\max}^{\mathrm{EtOH}}$ 273 mμ (ε 6400).

*Anal.* Calcd. for $C_{17}H_{15}IO_2$: C, 53.99; H, 3.99. Found: C, 54.17; H, 3.92.

**Methyl Ester of 1-Methyl-10-phenanthroic Acid (XIII, R = CH$_3$).**—The photolysis reaction on 2-methyl-2′-iodo-*cis*-stilbene-α-carboxylic acid methyl ester (XII, R = $CH_3$, 0.100 g., 0.00026 mole, m.p. 92–94°), in purified cyclohexane (475 ml.) for 4.5 hr., afforded a crystalline product (0.041 g., 62%), m.p. 90–94°. Recrystallization from aqueous ethanol afforded an analytical sample, m.p. 94–95°, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.82 μ.

*Anal.* Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.84; H, 5.93.

The melting point was not depressed by admixture with a sample obtained by methylation of the corresponding acid prepared by the procedure of Pschorr.[14]

**α-Nitro-2′-iodo-*cis*-stilbene (XVI).**—To a 10-ml. erlenmeyer flask were added phenylnitromethane (XIV, 0.274 g., 0.0020 mole), the *n*-propylidene base of *o*-iodobenzaldehyde (XV, 0.546 g., 0.0020 mole), and glacial acetic acid (5 ml.). The orange-yellow solution was allowed to stand at room temperature overnight. Addition of a few drops of water, cooling, and scratching with a glass rod induced crystallization. The yellow crystals were filtered and dried (0.324 g.), m.p. 55–58°. Recrystallization from ethanol afforded shiny prismatic yellow needles (0.297 g., 42%): m.p. 64–65°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 6.55, 7.50 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 314 mμ (ε 7600).

*Anal.* Calcd. for $C_{14}H_{10}INO_2$: C, 47.89; H, 2.87; N, 3.99. Found: C, 47.69; H, 3.10; N, 4.19.

**9-Nitrophenanthrene (XVII).**—Photolysis of α-nitro-2′-iodo-*cis*-stilbene (XVI, 0.100 g., 0.00028 mole, m.p. 64–65°) in cyclohexane (1000 ml.) required 2.5 hr. Evaporation of the solvent under reduced pressure afforded a brown oil (0.054 g.). Crystallization was induced by the addition of a few drops of ethanol and a yellow crystalline product was obtained (0.024 g., 40%), m.p. 114–116° (lit.[33] m.p. 116°).

**o-Toluoyl chloride (XIX)** was prepared by the method of Davies and Perkin,[34] b.p. 85–86° (22 mm.), in 81% yield (lit.[34] b.p. 213°).

**α-Bromo-*o*-toluoyl bromide (XX)** was prepared by the method of Davies and Perkin,[34] b.p. 135–140° (3.5 mm.), in 72% yield (lit.[34] b.p. 170–171° at 32 mm.).

**Methyl Ester of α-Bromo-*o*-toluic Acid (XXI).**—α-Bromo-*o*-toluoyl bromide (XX, 92.1 g., 0.355 mole, b.p. 135–140° at 3.5 mm.) was added dropwise to a previously cooled solution of anhydrous methanol (155 ml.). The reaction mixture was allowed to stand overnight in the refrigerator. It was then poured into ice water (300 ml.) and extracted with two 100-ml. portions of ether. The combined extracts were washed with water and 10% sodium bicarbonate solution and dried over magnesium sulfate. Evaporation of the ether afforded a colorless oil (78.5 g., 100%) $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.82 μ (ester carbonyl).

**2-Carbomethoxyphenylnitromethane (XXII).**—In a three-necked 500-ml. flask, provided with a mechanical stirrer, drying tube, and equilibrating funnel, was placed a slurry of silver nitrite (50 g., 0.32 mole) in anhydrous ether (150 ml.). The reaction flask and its contents were moved to a dark refrigerator room and allowed to equilibrate to the room temperature (4°). α-Bromo-*o*-toluic acid methyl ester (XXI, 45.8 g., 0.200 mole) was added dropwise to the stirred reaction mixture over a period of 30 min. The mixture was then stirred for 25 hr. at 4°. The inorganic salts were filtered: 60 g. of a yellow salt had formed which immediately turned black on contact with light. Concentration of the ethereal filtrate to about one-half of its volume and cooling in an acetone–Dry Ice bath afforded a colorless, shiny, crystalline material in the form of plates (10.50 g.). Further concentration of the ethereal solution afforded an additional 2.41 g. of product, m.p. 61–64.5°. The crystalline product was recrystallized from Skellysolve B to afford shiny, colorless plates (12.2 g., 31%), m.p. 64–65°. The infrared spectrum showed peaks at 5.82 (ester band), 6.44, and 7.29 μ (unconjugated nitro bands).

*Anal.* Calcd. for $C_9H_9NO_4$: C, 55.38; H, 4.65; N, 7.18. Found: C, 55.32; H, 4.77; N, 7.11.

**2-Carbomethoxy-2′-iodo-α-nitro-*cis*-stilbene (XXIII).**—To a 10-ml. erlenmeyer flask were added 2-carbomethoxyphenylnitromethane (XXII, 0.780 g., 0.0040 mole, m.p. 64–65°) and glacial acetic acid (2.5 ml.). The mixture was warmed gently to dissolve XXII, and, while stirring, the *n*-propylidene base of *o*-iodobenzaldehyde (XV, 1.09 g., 0.0040 mole) was added dropwise. The reaction mixture was heated for 1 min. at the boiling point and then quenched by pouring over ice. The water was decanted and the brown oil was crystallized by the addition of a few drops of ethanol (0.842 g.). This yellow product was recrystallized from ethanol, affording long yellow needles (0.785 g., 48%): m.p. 144–145°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.82, 6.55, 7.48 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 306 mμ (ε 9000).

*Anal.* Calcd. for $C_{16}H_{12}INO_4$: C, 46.96; H, 2.96; N, 3.42. Found: C, 47.11; H, 3.12; N, 3.33.

**Methyl Ester of 10-Nitro-1-phenanthroic Acid (XXIV).**—Irradiation of 2-carbomethoxy-2′-iodo-α-nitro-*cis*-stilbene (XXIII, 0.200 g., 0.0005 mole, m.p. 144–145°) in cyclohexane (1000 ml.) for 6 hr., followed by the usual work-up, afforded a brown oil (0.112 g.). This oil was chromatographed by preparative t.l.c. (silica gel G and chloroform elution), and the product obtained from the chromatography was crystallized from ethanol (0.056 g., 40% based on total starting material or 50% based on unrecovered starting material): m.p. 152–153°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.82, 6.56, 7.41 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 257.5 mμ (ε 36,800).

*Anal.* Calcd. for $C_{16}H_{11}NO_4$: C, 68.32; H, 3.94; N, 4.98. Found: C, 68.51; H, 4.09; N, 4.82.

**10-Nitro-1-phenanthroic Acid (XXV).**—In a 50-ml. round-bottom flask equipped with a water condenser were placed 1-carbomethoxy-10-nitrophenanthrene (XXIV, 36 mg., 0.00013 mole, m.p. 152–153°), methanol (15 ml.), and 20% aqueous potassium hydroxide (7 ml.). The yellow reaction mixture was allowed to reflux for 12 hr. in an oil bath. The methanol was evaporated under reduced pressure, water (10 ml.) was added, and the cooled solution was acidified with concentrated hydrochloric acid to congo red. The yellow product was filtered and dried (22 mg., m.p. 257–261°). Two successive recrystallizations from ethanol afforded tan, shiny crystals (0.017 g., 50%), m.p. 270–271°, undepressed upon admixture with a sample prepared by an alternate route[1]: $\lambda_{\max}^{\mathrm{KBr}}$ 5.90, 6.58, 7.40 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 256.5 mμ (ε 37,200).

*Anal.* Calcd. for $C_{15}H_9NO_4$: C, 67.41; H, 3.39; N, 5.24. Found: C, 67.57; H, 3.62; N, 5.34.

**2-Carbomethoxy-α-nitro-*cis*-stilbene (XXVII).**—In a 25-ml. erlenmeyer flask were added 2-carbomethoxyphenylnitromethane (XXII, 0.585 g., 0.0030 mole, m.p. 64–65°), *n*-propylidene base of benzaldehyde (0.819 g., 0.0030 mole), and glacial acetic acid (10 ml.). The yellow solution was allowed to stand undisturbed overnight at room temperature. The yellow crystalline material which had formed was filtered and dried (0.624 g., 75%), m.p. 88–92°. Recrystallization from ethanol afforded shiny yellow needles (0.586 g.): m.p. 94–96°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.82, 6.58, 7.52 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 315 mμ (ε 14,500).

*Anal.* Calcd. for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.95. Found: C, 68.02; H, 4.77; N, 4.94.

**2-Carbomethoxy-2′-chloro-α-nitro-*cis*-stilbene (XXVIII).**—In a 5-ml. erlenmeyer flask were placed 2-carbomethoxyphenylnitromethane (XXII, 0.195 g., 0.0010 mole, m.p. 64–65°), *n*-propylidene base of *o*-chlorobenzaldehyde (0.182 g., 0.0010 mole), and glacial acetic acid (1 ml.). The reaction mixture was heated to the boiling point for 1 min. and quenched by pouring over ice. After decantation of the water, the light yellow oil was crystallized by scratching with a glass rod (0.182 g., 57%). Recrystallization from ethanol gave a light yellow crystalline product (0.165 g.): m.p. 117–118°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.81, 6.55, 7.50 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 308 mμ (ε 10,300).

*Anal.* Calcd. for $C_{16}H_{12}ClNO_4$: C, 60.49; H, 3.81; N, 4.41. Found: C, 60.62; H, 3.74; N, 4.45.

**2-Carbomethoxy-3′-iodo-α-nitro-*cis*-stilbene (XXIX).**—2-Carbomethoxyphenylnitromethane (XXII, 0.780 g., 0.0040 mole, m.p. 64–65°) was dissolved in hot glacial acetic acid (2.5 ml.). The *n*-propylidene base of *m*-iodobenzaldehyde (1.09 g., 0.0040 mole) was added dropwise to the hot solution; the reaction was heated to the boiling point for 1 min. and quenched by pouring over ice. The light yellow oil which had formed was crystallized by the addition of a small amount of ethanol and scratching with a soft glass rod (1.21 g., m.p. 79–84°). Recrystallization from ethanol gave analytically pure material (1.14 g., 70%): m.p. 85–86°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.81, 6.55, 7.50 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 309 mμ (ε 8060).

*Anal.* Calcd. for $C_{16}H_{12}INO_4$: C, 46.96; H, 2.96; N, 3.42. Found: C, 47.07; H, 3.16; N, 3.61.

**3′-Iodo-α-nitro-*cis*-stilbene (XXX).**—A solution of phenylnitromethane (XIV, 0.274 g., 0.0020 mole) and *n*-propylidene base of 3-iodobenzaldehyde (0.546 g., 0.0020 mole) in glacial acetic acid (5 ml.) was allowed to stand at room temperature

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(33) J. Schmidt and E. Heinle, *Ber.*, **44**, 1488 (1911).

(34) W. Davies and W. H. Perkin, Jr., *J. Chem. Soc.*, **121**, 2202 (1922).

overnight. The reaction mixture was poured over ice, affording a viscous orange oil (0.422 g.). This oily product was chromatographed on silica gel (chloroform elution) affording a bright yellow oil which was crystallized by the addition of ethanol (0.420 g., 60%): m.p. 68–69°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 6.56, 7.51 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 310 mμ (ε 11,950).

*Anal.* Calcd. for $C_{14}H_{10}INO_2$: C, 47.89; H, 2.87; N, 3.99. Found: C, 48.37; H, 2.85; N, 4.21.

**2-Carbomethoxy-4′-iodo-α-nitro-*cis*-stilbene (XXXI).**—2-Carbomethoxyphenylnitromethane (XXII, 0.390 g., 0.0020 mole, m.p. 64–65°) was dissolved in hot glacial acetic acid (3 ml.). The *n*-propylidene base of 4-iodobenzaldehyde (0.508 g., 0.0020 mole) was added dropwise to the hot solution. The yellow mixture was then heated to the boiling point and almost all the acetic acid allowed to evaporate until a syrupy orange-red mass remained in the flask. This product was chromatographed by preparative t.l.c. on silica gel $HF_{254+366}$ (chloroform elution), and a major yellow band afforded a yellow oil (0.322 g.). This material was extracted with 40% sodium bisulfite solution to remove aldehyde responsible for a positive 2,4-dinitrophenylhydrazone (2,4-DNP) test. The yellow oil which remained was extracted with chloroform, washed with water, and dried over sodium sulfate. Evaporation of the solvent afforded a thick yellow oil which was crystallized by the addition of a small amount of ethanol (0.197 g.), m.p. 94–95°. This product was recrystallized twice from ethanol and gave shiny yellow crystals: m.p. 98–99°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.82, 6.56, 7.50 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 229.5 mμ (ε 22,000), 328 mμ (ε 17,800).

*Anal.* Calcd. for $C_{16}H_{12}INO_4$: C, 46.96; H, 2.96; N, 3.42. Found: C, 47.35; H, 2.84; N, 3.56.

**Piperonyl alcohol (XXXIII)** was prepared by the method of Larsson,[20] m.p. 54–55°, in quantitative yield (lit.[20] m.p. 54–55°).

**6-Bromopiperonyl bromide (XXXIV)** was prepared by the method of Barthel and Alexander,[21] m.p. 92–93°, in 68% yield (lit.[21] m.p. 92–93°).

**2-Bromo-4,5-methylenedioxytoluene (XXXV).**—In a three-necked, 1-l., round-bottom flask equipped with a mechanical stirrer, water condenser with drying tube, and equilibrating dropping funnel were added lithium aluminum hydride (10.2 g., 0.264 mole) and tetrahydrofuran (150 ml.). To the stirring suspension was added XXXIV (61.5 g., 0.205 mole, m.p. 92–93°) dissolved in tetrahydrofuran (200 ml.) over a period of 1 hr. The mixture was refluxed for 2 hr. on the steam bath. After cooling, aqueous tetrahydrofuran (10%, 80 ml.) was added cautiously to decompose the excess lithium aluminum hydride, followed by 10% hydrochloric acid (75 ml.). The salts were filtered and washed thoroughly with ether, and the combined filtrates were dried over anhydrous sodium sulfate. The light yellow oil (44.2 g.) remaining after the evaporation of the solvent was distilled under vacuum. A colorless oil, which crystallized on cooling, was obtained (34.15 g., 77%), b.p. 70–73° (0.3 mm.), m.p. 34–36° (lit.[35] m.p. 34°).

**2-Methyl-4,5-methylenedioxybenzoic Acid (XXXVI).**—To a three-necked, 1-l., round-bottom flask equipped with a mechanical stirrer, water condenser with drying tube, and inlet for nitrogen was added XXXV (21.5 g., 0.10 mole, m.p. 34–36°) in anhydrous ether (400 ml.). The solution was cooled to −78° in an acetone–Dry Ice bath and kept under an atmosphere of nitrogen throughout the entire reaction. A hexane solution of *n*-butyllithium (45 ml., 15.13%) was added in small portions by means of a hypodermic syringe through a rubber cap inlet. The addition required 90 min. The pale yellow solution was then stirred for an additional 3 hr. at −78° and poured over a slurry of powdered Dry Ice in ether (400 ml.). The white suspension was allowed to remain at room temperature for 4 hr. Two 100-ml. portions of water were used to extract the product. The pink aqueous extract was washed with ether, freed of traces of ether under reduced pressure, cooled, and acidified with concentrated hydrochloric acid to congo red. The white, fluffy precipitate was filtered, washed with water, and dried over phosphorus pentoxide (7.34 g., 41%). Three recrystallizations from ethyl acetate afforded analytically pure product: m.p. 199–200°; $\lambda_{\max}^{\mathrm{Nujol}}$ 5.91, 10.72 μ.

*Anal.* Calcd. for $C_9H_8O_4$: C, 60.00; H, 4.48. Found: C, 60.21; H, 4.69.

**2-Methyl-4,5-methylenedioxybenzoyl Chloride (XXXVII).**—In a 25-ml. round-bottom flask, fitted with a water condenser with drying tube and a magnetic stirrer, was placed a suspension of 2-methyl-4,5-methylenedioxybenzoic acid (XXXVI, 1.62 g., 0.0090 mole, m.p. 199–200°) in dry benzene (10 ml.). Oxalyl chloride (5.4 ml.) was added in small portions and the mixture was stirred at room temperature for 2 hr. The clear yellow solution which had formed was refluxed 15 min. and the benzene was evaporated under reduced pressure, yielding a colorless crystalline product (1.75 g., 98%), $\lambda_{\max}^{\mathrm{Nujol}}$ 5.68 μ.

**2-Bromomethyl-4,5-methylenedioxybenzoyl Bromide (XXXVIII).**—The acid chloride XXXVII (1.75 g., 0.00884 mole) dissolved in carbon tetrachloride (10 ml.) was brominated, in the presence of radiation from a 200-w. tungsten lamp, by the dropwise addition of a solution of bromine in carbon tetrachloride (9 ml. of a solution made from 5.5 ml. of liquid bromine in 94.5 ml. of carbon tetrachloride). The red color of bromine was bleached immediately on contact with the refluxing solution, and the evolution of a hydrogen halide gas was observed. After the addition of bromine was completed, the mixture was allowed to stir and reflux for an additional 15 min., and the solvent was removed under reduced pressure. A thick yellowish oil was obtained (1.83 g., 64%).

**Methyl Ester of 2-Bromomethyl-4,5-methylenedioxybenzoic Acid (XXXIX).**—The dibromo product XXXVIII (1.83 g., 0.0057 mole) was cooled in an ice bath and, while stirring, absolute methanol (15 ml.) was added in small portions. The resulting yellow solution was concentrated to roughly one-half of its original volume and cooling afforded a colorless crystalline precipitate (1.46 g., m.p. 74–79°). Two successive recrystallizations from Skellysolve B afforded shiny needles (1.39 g., 89%), m.p. 84–86°. This material gave a positive Beilstein test, a positive silver nitrate test, and a positive sodium iodide in acetone test for alkyl halogen. The n.m.r. spectrum showed a new signal at τ 5.05 ($-CH_2-Br$).

*Anal.* Calcd. for $C_{10}H_9BrO_4$: C, 43.98; H, 3.32. Found: C, 44.10; H, 3.46.

**2-Carbomethoxy-4,5-methylenedioxyphenylnitromethane (XLI).**—A slurry of silver nitrite (1.54 g., 0.010 mole) in anhydrous ether (25 ml.) was placed in a 100-ml., round-bottom, three-necked flask equipped with a magnetic stirrer and dropping funnel. The mixture was cooled to 0° and kept in complete darkness. The bromo ester XXXIX (1.37 g., 0.0050 mole, m.p. 84–86°) in anhydrous ether (20 ml.) was added dropwise to the cold suspension over a period of 30 min. After stirring in the dark at 0° for 24 hr., the ether mixture was filtered free of inorganic salts (1.56 g., yellow salts which darkened immediately upon exposure to light). The filtrate was reduced to one-half of its volume and cooled. The white product was filtered, giving 0.287 g., m.p. 127–129°. Thin layer chromatography on silica gel G (chloroform elution) showed one spot: $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.84, 6.45, 7.28 μ. The remaining other portion was evaporated, affording a semicrystalline material (0.753 g.). This product was fractionally crystallized from a Skellysolve B–chloroform mixture to afford an additional 0.247 g. of product, m.p. 127–129°. The product was recrystallized from Skellysolve B and chloroform to afford an analytical sample, m.p. 130–130.5°.

*Anal.* Calcd. for $C_{10}H_9NO_6$: C, 50.21; H, 3.79; N, 5.86. Found: C, 50.32; H, 3.91; N, 5.95.

The remaining 0.462 g. of crystalline material, m.p. 188–190°, had a lower $R_f$ value on t.l.c. and showed a peak at 5.69 μ (lactone) in the infrared. This material was characterized as 4,5-methylenedioxyphthalide (XL) by mixture melting point and infrared spectrum superimposable upon that of material prepared according to the method of Stevens and Robertson.[22,23]

**2-Nitro-6-aminotoluene (XLIII)** was prepared by the method of Brady and Taylor,[36] m.p. 90–92°, in 90% yield (lit.[36] m.p. 92°).

**2-Methyl-3-nitrophenol (XLIV)** was prepared by the method of Noelting,[37] m.p. 141–143°, in 58% yield (lit.[37] m.p. 145°).

**2-Nitro-6-methoxytoluene (XLV)** was prepared by the method of Simonsen and Nayak,[38] m.p. 54–55.5°, in 56% yield (lit.[38] m.p. 52–53°).

**2-Nitro-6-methoxybenzyl bromide (XLVI)** was prepared by the method of Kupchan and Merianos,[24] m.p. 65–67° (crude), in quantitative yield (lit.[24] m.p. 70–71°).

**1-(2-Nitro-6-methoxybenzyl)pyridinium bromide (XLVII)** was prepared by the method of Kupchan and Merianos,[24] m.p. 179–182°, in 82% yield (lit.[24] m.p. 178–180°).

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(35) M. Tomita, E. Fujita, and T. Abe, *J. Pharm. Soc. Japan*, **72**, 384 (1952).

(36) O. L. Brady and A. Taylor, *J. Chem. Soc.*, **117**, 876 (1920).

(37) E. Noelting, *Ber.*, **37**, 1015 (1904).

(38) J. L. Simonsen and M. Nayak, *J. Chem. Soc.*, **107**, 828 (1915).

**2-Nitro-6-methoxyphenyl-N-*p*-dimethylaminophenyl nitrone (XLVIII)** was prepared by the method of Kupchan and Merianos,[24] m.p. 162–165°, in 79% yield (lit.[24] m.p. 162–165°).

**2-Nitro-6-methoxybenzaldehyde (XLIX)** was prepared by the method of Kupchan and Merianos,[24] m.p. 110–111°, in 77% yield (lit.[24] m.p. 110–111°).

**2-Nitro-6-methoxybenzaldoximes (L and LI).**—In a 500-ml. round-bottom flask equipped with a water condenser were placed 2-nitro-6-methoxybenzaldehyde (XLIX, 10.8 g., 0.0597 mole, m.p. 110–111°), hydroxylamine hydrochloride (11 g.), pyridine (11 ml.), and ethanol (110 ml.). The mixture was refluxed on a steam bath for 1 hr. and poured over ice. A yellowish green crystalline product was filtered and dried (11.2 g., 96%), m.p. 154–155°. Thin layer chromatography on silica gel G (10% ethanol in chloroform elution) showed this product to be a mixture of two closely related compounds, having similar $R_f$ values. Separation was effected by preparative t.l.c. and the two products, L and LI, were obtained in pure form.

Recrystallization of the less polar compound (L) from acetone–chloroform afforded shiny, short, prismatic yellow needles: m.p. 168–170°; $\lambda_{\max}^{\mathrm{KB}}$ 3.08, 6.20 $\mu$.

The more polar product LI was also recrystallized from acetone–chloroform and afforded colorless needles: m.p. 197–201°; $\lambda_{\max}^{\mathrm{KBr}}$ 3.10, 6.00, 6.20 $\mu$.

*Anal.* Calcd. for $C_8H_8N_2O_4$ (L): C, 48.98; H, 4.11; N, 14.28. Found: C, 49.04; H, 4.22; N, 14.45.

*Anal.* Calcd. for $C_8H_8N_2O_4$ (LI): C, 48.98; H, 4.11; N, 14.28. Found: C, 48.86; H, 3.92; N, 14.32.

**2-Amino-6-methoxybenzaldoxime (LII).**—A cold suspension of ferrous hydroxide was prepared by the dropwise addition of a solution of sodium hydroxide (1.0 g., 0.0260 mole, in 10 ml. of water) to ferrous sulfate heptahydrate (3.55 g., 0.0128 mole) in water (10 ml.). The mixture of nitro oximes L and LI (0.400 g., 0.0020 mole) dissolved in 5% sodium hydroxide solution (2 ml.) was added dropwise, with vigorous stirring, to the suspension. The mixture, which turned dark brown, was allowed to stir in the cold for an additional 15 min. and centrifuged. The water was decanted and treated with carbon dioxide until the pH remained constant (pH ~6). The residual ferric salt mixture and the $CO_2$-treated water layer were extracted with chloroform (three 250-ml. portions) and the extract was dried over sodium sulfate. Evaporation of the solvent gave a light brown solid material (0.274 g.). Recrystallization from benzene afforded shiny colorless needles (0.224 g., 68%), m.p. 184.5–185.5°.

*Anal.* Calcd. for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.10; H, 6.07; N, 16.82.

**2-Iodo-6-methoxybenzaldehyde (LIII).**—To a stirred paste of concentrated hydrochloric acid (5 ml.), cooled in an acetone–Dry Ice bath, was added dropwise a solution of 2-amino-6-methoxybenzaldoxime (LII, 0.500 g., 0.0030 mole, m.p. 184.5–185.5°) in purified dioxane (5 ml.). The tan suspension was then allowed to warm up to −10° in a salt–ice bath and diazotized by the dropwise addition of sodium nitrite (0.750 g., 0.0100 mole) in water (4 ml.). The mixture turned to a yellow brown solution and was stirred for an additional 30 min. Potassium iodide (1.25 g., 0.0750 mole) in water (2 ml.) was added, and the black oily mixture was stirred overnight. The reaction mixture was extracted with three 50-ml. portions of chloroform; the extract was washed with 10% sodium hydroxide solution and water and dried over magnesium sulfate. Evaporation of the solvent gave a dark brown oil (0.452 g.). Preparative t.l.c. on silica gel G (chloroform elution) gave mainly two products. The desired iodoaldehyde LIII (0.098 g.) was obtained as a low-melting solid, m.p. 36–38°, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.92 $\mu$. It was characterized by analysis of the 2,4-dinitrophenylhydrazone derivative, m.p. 255–256.5°.

*Anal.* Calcd. for $C_{14}H_{11}IN_4O_5$: C, 38.03; H, 2.51; N, 12.67. Found: C, 38.20; H, 2.78; N, 13.28.

The second product LIV, (0.102 g.), m.p. 73–74° from Skellysolve B, was identified as 2-azido-6-methoxybenzaldehyde: $\lambda_{\max}^{\mathrm{CHCl_3}}$ 4.50, 4.70, 5.94 $\mu$.

*Anal.* Calcd. for $C_8H_7N_3O_2$: C, 53.92; H, 3.96; N, 23.60. Found: C, 53.94; H, 4.03; N, 23.71.

**2-Carbomethoxy-4,5-methylenedioxy-2′-iodo-6′-methoxy-α-nitro-*cis*-stilbene (LVI).**—In a 10-ml. erlenmeyer flask was placed a mixture of 2-carbomethoxy-4,5-methylenedioxyphenylnitromethane (XLI, 0.239 g., 0.0010 mole, m.p. 130–130.5°), *n*-propylidene base of 2-iodo-6-methoxybenzaldehyde (LV, 0.393 g., 0.0013 mole), and glacial acetic acid (5 ml.). The mixture was heated to boiling on a hot plate and the acetic acid was allowed to evaporate to almost dryness. To the cooled dark brown oil were added a few drops of ethanol, and the yellow solid formed was filtered and dried (0.290 g.). Chromatography of the mother liquor on silica gel afforded an additional 60 mg. of product. Recrystallization from ethanol gave yellow crystals (0.310 g., 64%), m.p. 150–151°. Two additional recrystallizations from ethanol gave an analytical sample: m.p. 154–155°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.85, 6.55, 7.50 $\mu$; $\lambda_{\max}^{\mathrm{EtOH}}$ 304 m$\mu$ ($\epsilon$ 9400).

*Anal.* Calcd. for $C_{18}H_{14}INO_7$: C, 44.75; H, 2.92; N, 2.90. Found: C, 45.22; H, 2.82; N, 3.05.

**Methyl Ester of Aristolochic Acid I (LVII).**—A solution of LVI (0.100 g., 0.00021 mole, m.p. 154–155°) in purified cyclohexane (475 ml.) was photolyzed in the usual manner. Evaporation of the solvent after 2 hr. of irradiation afforded a brown oil (0.054 g.). Preparative t.l.c. on silica gel $HF_{254+366}$ (elution with 5% methanol in chloroform) afforded a yellow crystalline product (0.040 g., 54%), m.p. 276–278°. Recrystallization from ethanol afforded shiny yellow needles (0.037 g., m.p. 280–283°) (lit.[39] m.p. 281).

**Aristolochic acid I (I)** was prepared by hydrolysis of ester LVII according to the method of Pailer and Schleppnik,[39] m.p. 275–277°. The melting point was not depressed by admixture with an authentic sample. The infrared spectrum (KBr) was superimposable upon that of the authentic sample: $\lambda_{\max}^{\mathrm{EtOH}}$ 250 m$\mu$ ($\epsilon$ 27,000), 318 (12,000), 390 (6500).

**2-Carbomethoxy-4,5-methylenedioxy-2′-iodo-α-nitro-*cis*-stilbene (LVIII).**—In a 10-ml. erlenmeyer flask was placed a mixture of 2-carbomethoxy-4,5-methylenedioxyphenylnitromethane (XLI, 0.120 g., 0.0005 mole, m.p. 130–130.5°), *n*-propylidene base of *o*-iodobenzaldehyde (XV, 0.411 g., 0.0015 mole), and glacial acetic acid (5 ml.). The mixture was heated to the boiling point for 5 min. and quenched by pouring over ice. The water solution was decanted and the yellow oil was crystallized by the addition of a few drops of ethanol (0.134 g.). The product was chromatographed on silica gel G plates (chloroform elution). The major yellow band, after suitable extraction and evaporation of the solvent, afforded a thick, bright yellow oil. Crystallization was induced by the addition of ethanol (0.085 g., 38%), m.p. 131–133°.

*Anal.* Calcd. for $C_{17}H_{12}INO_6$: C, 45.06; H, 2.67; N, 3.09. Found: C, 45.37; H, 2.77; N, 3.07.

**Methyl Ester of Aristolochic Acid II (LIX).**—Irradiation of 2-carbomethoxy-4,5-methylenedioxy-2′-iodo-α-nitro-*cis*-stilbene (LVIII, 0.063 g., 0.00014 mole, m.p. 131–133°) in cyclohexane (450 ml.) for 1 hr., followed by the usual work-up, afforded a brown, oily material (0.037 g.). Preparative t.l.c. on silica gel G (chloroform elution) afforded a yellow crystalline solid as part of the major yellow band (0.012 g., 26%), m.p. 270–275°. Recrystallization from methanol afforded shiny needles (9 mg.): m.p. 274–275° (lit.[39] m.p. 274°); $\lambda_{\max}^{\mathrm{KBr}}$ 5.82, 6.60, 7.42 $\mu$; $\lambda_{\max}^{\mathrm{EtOH}}$ 252 m$\mu$ (log $\epsilon$ 4.58), 298 m$\mu$ (log $\epsilon$ 4.18) [lit.[39] $\lambda_{\max}^{\mathrm{EtOH}}$ 252 m$\mu$ (log $\epsilon$ 4.64), 298 m$\mu$ (log $\epsilon$ 4.22)].

**2-Carbomethoxy-2′-iodo-6′-methoxy-α-nitro-*cis*-stilbene (LX).**—In a 10-ml. erlenmeyer flask was placed a mixture of 2-carbomethoxyphenylnitromethane (XXII, 0.293 g., 0.0015 mole, m.p. 64–65°), *n*-propylidene base of 2-iodo-6-methoxybenzaldehyde (LV, 0.453 g., 0.0015 mole), and glacial acetic acid (5 ml.). The mixture was heated to boiling and the acetic acid was allowed to evaporate almost to dryness. Addition of a small amount of ethanol led to the formation of a yellow solid product (0.421 g., 64%), m.p. 85–92°. Several recrystallizations from ethanol gave an analytical sample: m.p. 100–101°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.82, 6.55, 7.48 $\mu$; $\lambda_{\max}^{\mathrm{EtOH}}$ 314 m$\mu$ ($\epsilon$ 12,800).

*Anal.* Calcd. for $C_{17}H_{14}INO_5$: C, 46.49; H, 3.21; N, 3.19. Found: C, 46.54; H, 3.43; N, 3.42.

**1-Carbomethoxy-8-methoxy-10-nitrophenanthrene (LXI).**—Photolysis of 2-carbomethoxy-2′-iodo-6′-methoxy-α-nitro-*cis*-stilbene (LX, 0.050 g., 0.00011 mole, m.p. 100–101°) in cyclohexane (475 ml.) for 2 hr., followed by the usual work-up, afforded a brown oily residue (0.031 g.). Preparative thin layer chromatography on silica gel $HF_{254+366}$ (10% methanol in chloroform elution) afforded a yellow crystalline material (0.020 g., 60%), m.p. 173–175°. Recrystallization from ethanol gave fine, shiny yellow needles (0.017 g.): m.p. 175–176°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.81, 6.58, 7.40 $\mu$; $\lambda_{\max}^{\mathrm{EtOH}}$ 230 m$\mu$ ($\epsilon$ 35,000), 253.5 (24,500), 279 (13,000).

*Anal.* Calcd. for $C_{17}H_{13}NO_5$: C, 65.59; H, 4.21; N, 4.50. Found: C, 65.29; H, 4.41; N, 4.47.

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(39) M. Pailer and A. Schleppnik, *Monatsh.*, **88**, 367 (1957).

**6-Nitropiperonal** (**LXII**) was prepared by the method of Parijs,[40] m.p. 98–98.5°, in 51% yield (lit.[40] m.p. 98°).

**6-Aminopiperonal** (**LXIII**) was prepared by the method of Campbell,[41] m.p. 106–108°, in 62% yield (lit.[41] m.p. 107–108°).

**6-Iodopiperonal** (**LXIV**) was prepared by the method of Rilliet and Kreitmann,[42] m.p. 112–113°, in 52% yield (lit.[42] m.p. 111°).

**2-Carbomethoxy-2′-iodo-4′,5′-methylenedioxy-α-nitro-*cis*-stilbene** (**LXVI**).—In a 5-ml. erlenmeyer flask was placed a mixture of 2-carbomethoxyphenylnitromethane (XXII, 0.098 g., 0.0005 mole, m.p. 64–65°), *n*-propylidene base of 6-iodopiperonal (LXV, 0.150 g., 0.0005 mole), and glacial acetic acid (4 ml.). The mixture was heated on a hot plate and the acetic acid was evaporated almost to dryness. The resulting dark brown oil was chromatographed on silica gel $HF_{254+366}$ plates (chloroform elution) and gave, after appropriate work-up, yellow-orange prisms (0.072 g., 32%), m.p. 118–119°. An analytical sample was prepared by recrystallization from ethanol: m.p. 118–119°; $\lambda_{\max}^{CHCl_3}$ 5.82, 6.56, 7.50, 10.70 μ; $\lambda_{\max}^{EtOH}$ 370 mμ (ε 8700).

*Anal.* Calcd. for $C_{17}H_{12}INO_6$: C, 45.06; H, 2.67; N, 3.09. Found: C, 45.14; H, 2.78; N, 3.15.

**1-Carbomethoxy-6,7-methylenedioxy-10-nitrophenanthrene** (**LXVII**). — 2-Carbomethoxy-2′-iodo-4′,5′-methylenedioxy-α-nitro-*cis*-stilbene (LXVI, 0.0720 g., 0.00016 mole, m.p. 118–119°) was photolyzed under the usual conditions for 3 hr. The cyclohexane (1000 ml.) and traces of iodine were removed under reduced pressure affording a brown oily residue (0.039 g.). Preparative t.l.c. on silica gel $HF_{244+366}$ (chloroform elution) afforded fine yellow needles (0.020 g., 39%): m.p. 254–255°; $\lambda_{\max}^{KBr}$ 5.85, 6.58, 7.45, 10.65 μ; $\lambda_{\max}^{EtOH}$ 234 mμ (ε 18,400), 268 (20,300), 282 (17,800), 357 (4900).

*Anal.* Calcd. for $C_{17}H_{11}NO_6$: C, 62.77; H, 3.41; N, 4.31. Found: C, 62.69; H, 3.61; N, 4.29.

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[40] A. H. Parijs, *Rec. trav. chim.*, **49**, 17 (1930).

[41] K. N. Campbell, *J. Org. Chem.*, **16**, 1736 (1951).

[42] A. Rilliet and L. Kreitmann, *Helv. Chim. Acta*, **4**, 588 (1921).

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# Synthesis of Polyferrocenylene[1]

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Polyferrocenylene was formed when cobaltous chloride or an organic halide was added to lithiated ferrocene. The direct bonding of ferrocene nuclei in the polymerization reactions is accounted for by coupling of ferrocenyl radicals. Identification of ferrocene derivatives by low and high voltage mass spectrometry is demonstrated.

Biferrocenyl was first detected in the reaction products of trialkylchlorosilanes with lithiated ferrocene.[2,3] Since then biferrocenyl has been synthesized using Ullmann coupling, reaction of diferrocenylmercury with silver, ferrocenylmagnesium bromide with cobaltous chloride, and other methods.[4] Korshak and co-workers[5] obtained polyferrocenylene by heating ferrocene with *t*-butyl hydroperoxide. Rausch[6] reported polyferrocenylene in thermal decomposition products of mercury-bridged ferrocenes $(C_{10}H_{10}FeHg)_x$. Nesmeyanov and co-workers[7] obtained some polyferrocenylene in an Ullmann coupling where bromo- and 1,1′-dibromoferrocene were used.

In this paper we report that lithioferrocenes react readily with cobaltous chloride in the absence of any organic halide. The reaction gave polyferrocenylene. We also found that ferrocenyl coupling takes place when organic halides are added to lithiated ferrocene. Benzyl chloride was especially effective for promoting polyferrocenylene formation. Such polyferrocenylenes were found to consist of biferrocenyl and higher ferrocenyl coupling products.

**Lithiated Ferrocene and Cobaltous Chloride.**—Exothermic reaction of anhydrous cobaltous chloride with lithioferrocenes[8] in ether–tetrahydrofuran, followed by stirring at room temperature and hydrolysis, resulted in polyferrocenylene (I). Lithioferrocenes which had been synthesized by using the largest excess of *n*-butyllithium gave the highest yield (74.6%) of polyferrocenylene (Table I).

$$C_5H_5FeC_5H_5 \xrightarrow[\quad]{\substack{1.\ n\text{-}C_4H_9Li \\ 2.\ CoCl_2 \\ 3.\ H_2O}} H\text{+}C_5H_4FeC_5H_4\text{+}_nH \qquad \underset{n \geq 2}{\text{I}}$$

TABLE I

EFFECT OF REAGENT CONCENTRATION ON POLYFERROCENYLENE YIELDS. LITHIOFERROCENES AND COBALTOUS CHLORIDE REACTIONS

| Moles of reagents | | | | Polyferrocenylene | |
|---|---|---|---|---|---|
| Ferrocene | *n*-Butyllithium | Cobaltous chloride | Ferrocene recovery, % | Yield,[a] % | Av. mol. wt. |
| 0.1 | 1.0 | 0.2 | 21.6 | 74.6 | 985 |
| 0.1 | 0.5 | 0.2 | 35.0 | 51.5 | 1434 |
| 0.1 | 0.37 | 0.3 | 29.8 | 33.8 | 455 |
| 0.1 | 0.25 | 0.2 | 43.0 | 21.6 | 512 |

[a] The calculation of yields is based on ferrocene.

Earlier in this laboratory we found that low voltage mass spectrometry of ferrocene and many of its derivatives gives intense molecule ion peaks with little or no fragmentation.[9] The method was useful for identification of ferrocene derivatives also in this work. Within the working range (up to a mass of about 700), I gave the following molecular ion peaks: ferrocene (*m*/*e* 186), cyclopentadienylferrocene (*m*/*e* 250), biferrocenyl (*m*/*e* 368, 370, 371, and 372), and terferrocenyl (*m*/*e* 554) (Table II).

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[1] Presented in part before the Division of Organic Chemistry, 148th National Meeting of the American Chemical Society, Chicago, Ill., 1964.

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[4] For a review of the literature, see M. D. Rausch, *Can. J. Chem.*, **41**, 1289 (1963).

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[9] D. J. Clancy and I. J. Spilners, *Anal. Chem.*, **34**, 1839 (1962).