Photocyclizations of α-(1-Cyclohexenyl)cinnamic Esters

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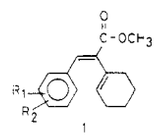
The photocyclizations of some α-(1-cyclohexenyl)cinnamic acid esters are described. Under oxidative conditions 5,6,7,8-tetrahydrophenanthrenes are formed in good yield. Under anaerobic conditions hexahydrophenanthrenes are formed. Their structure and the mechanisms of formation are discussed.

The photochemical cyclization of stilbenes into 9,10-dihydrophenanthrene derivatives under nonoxidative conditions has been examined by several authors.[1] In a previous paper[2] some of us clarified the mechanism for the cyclization of methyl α-phenylcinnamate (a) to 9-carbomethoxy-9,10-dihydrophenanthrene (f) (Scheme I). Kinetic studies revealed that the reaction occurs via the 4a,4b-dihydrophenanthrene derivative b, and it was established that the rearrangement b → f does not involve a photochemical 1,3-suprafacial shift. In a polar solvent a protonation–deprotonation reaction gives rise to c, which is in a tautomeric equilibrium with 4a,9-dihydrophenanthrene d. These reaction steps are decisive for the formation of the 9,10-dihydrophenanthrene. A necessary condition for this reaction is not only the presence of an enolizable group at C-9 of b but also a suitable source of hydrogen atoms in the medium (e.g., an alcohol as solvent) because the final conversion of d into 9,10-dihydrophenanthrene (f) proceeds via a radical reaction, which is probably photochemically induced.

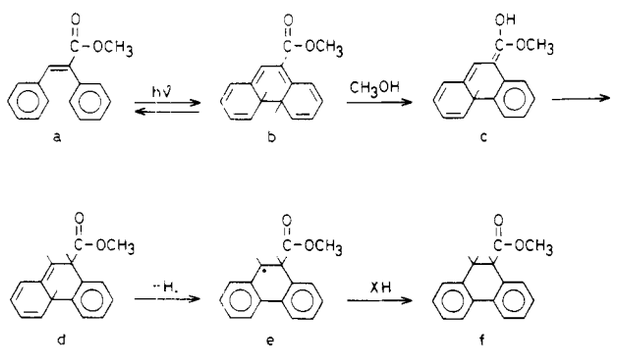
In a parallel study an effort was made to extend the synthetic utility of this type of reaction to the photocyclizations of various methyl α-(1-cyclohexenyl)cinnamates (**1a–c**).



a) $R_1 = H$, $R_2 = CF_3$ (4)
b) $R_1 = R_2 = Cl$ (2,4)
c) $R_1 = R_2 = OCH_3$ (3,5)

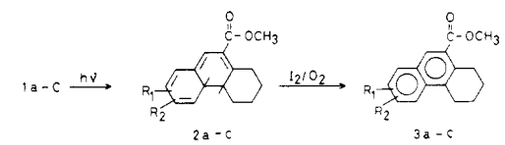
Hayward and Leznoff,[3] in an investigation of the photoreactivity of 1,4-diarylbutadienes, have shown that these compounds undergo photodehydrocyclizations which correspond to the reaction of stilbenes on irradiation in the presence of an oxidant, but the 4-aryl residue seems to be unnecessary for this type of reaction.[4] Recently, the intermediacy of a previously proposed[4] dihydro intermediate in this reaction was further substantiated.[5] Therefore, it could be expected

Scheme I



that the photolysis of compounds **1a–c** under oxidative conditions should proceed according to a scheme (Scheme II) which is formally analogous to the stilbene–phenanthrene photodehydrocyclization.

Scheme II



The fate of the intermediate **2a–c** under nonoxidative conditions had not been studied previously, and it seemed worthwhile to compare its reactivity with that of the corresponding α-carbomethoxy-4a,4b-dihydrophenanthrene intermediate in the photocyclization of methyl α-phenylcinnamates.[2]

Synthesis

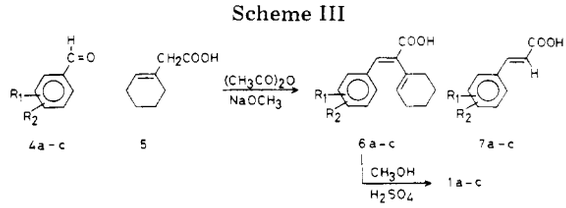
The cinnamates **1a–c** were readily prepared by the condensation of the benzaldehydes **4a–c** with 1-cyclohexenylacetic acid (**5**) and subsequent esterification of the resulting acid (**6**). The yields of the desired condensation products varied from 20 to 84%, depending upon the amount of acetic anhydride and the nature of the benzaldehyde used; with a large molar excess of the anhydride a competitive condensation between the aldehyde and the solvent led to substantial amounts of cinnamic acids (**7**) (Scheme III).

Oxidative Photocyclizations

Irradiation of the cinnamates **1a–c** in methanol through quartz and in the presence of iodine and air gave the expected 5,6,7,8-tetrahydrophenanthrenes **3a–c** in good yields (62–88%) and as the only products (Scheme II). The structures were established by elemental analyses and spectral evidence. NMR spectra indicated in all cases the proper ratio of aromatic, allylic, and aliphatic protons (see Experimental Section). The infrared spectra were also clearly indicative of α,β-unsaturated carboxylic esters.

Irradiations under similar conditions using a Pyrex filter gave no reaction. It is remarkable that the yields are high compared with those in the diphenylbutadiene cyclizations.[3]

Scheme III



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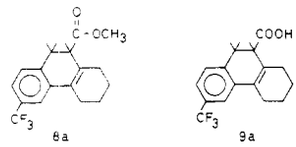
Nonoxidative Photocyclizations

Irradiations of **1a–c** in methanol through quartz and under nitrogen gave different results, depending on the aromatic substitution of the parent compound. In every case, the photochemical nature of the reactions was established by control irradiations in which Pyrex filters were used. In these latter instances only starting materials were recovered in quantitative yields. The results with each compound will be discussed separately.

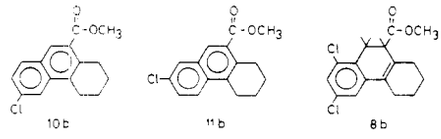
A. Methyl α-(1-Cyclohexenyl)-4′-trifluoromethylcinnamate (1a). The nonoxidative irradiation of **1a** gave, after workup, three compounds in 57, 24, and 5% yield, respectively. The main product showed an unconjugated ester carbonyl band (1745 cm^{-1}) in its IR spectrum. The NMR spectrum indicated the absence of vinyl protons. The occurrence of an ABC pattern in the NMR spectrum at δ 2.95 (dd, J_{AB} = 13.5, J_{AC} = 6 Hz), 3.18 (dd, J_{AB} = 13.5, J_{BC} = 3.5 Hz), and 3.02 (dd, J_{AC} = 6, J_{BC} = 3.5 Hz) is completely consistent with structure **8a**. The second product appeared to be an acid:



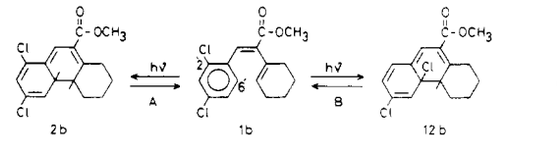
IR ν_{max} 1710 cm^{-1}; UV λ_{max} 275, 225 nm. The ABC pattern in its NMR spectrum was badly resolved, even at 220 MHz; δ 2.99 (s ?), 3.19 and 2.98 (possible dd). The compound must be **9a,** however, since the same product was obtained by basic hydrolysis of **8a.** It is supposed that **8a** is hydrolyzed during column chromatography. The third product appeared to be **3a,** which arises from **1a** under oxidative conditions. This might be due to the residual oxygen present in the solvent.

The structure of the main product suggests that it arises from an initially formed photocyclization product **2a** via similar rearrangements as those leading from 9-carbomethoxy-4a,4b-dihydrophenanthrenes to 9-carbomethoxy-9,10-dihydrophenanthrenes in the nonoxidative photocyclization of stilbene derivatives.[2] The similarity was further substantiated by irradiation of **1a** in CD_3OD. The principal product had an NMR spectrum which showed the disappearance of the signal at δ 3.02 (H_c) and the loss of one proton intensity in the combined positions H_A and H_B. The signals for H_A and H_B also collapse to doublets with $J_{AB} \sim 2$ Hz (deuterium coupling). Apparently the rearrangements proceed through the intermediacy of the solvent, leading to a mixture of *cis*- and *trans*-deuterio compounds.

B. Methyl α-(1-Cyclohexenyl)-2′,4′-dichlorocinnamate (1b). Irradiation of **1b** in degassed methanol solution gave one major product, a small amount of the oxidative product **3b,** and a considerable amount of tar. The IR spectrum of the major product indicated a conjugated ester carbonyl (1720 cm^{-1}). Both mass spectrum and elemental analysis showed only one chlorine and fit the formula $C_{16}H_{15}ClO_2$. The NMR spectrum (220 MHz) showed four aromatic (and/or vinyl) protons, two of which occurred as an AB quartet, indicative of two adjacent aromatic protons. One of these was coupled to another proton; δ 7.98 (s), 7.57 (d, J = 9 Hz), 7.26 (dd, J = 9, J' = 1.5 Hz), 7.76 (d, J' = 1.5 Hz). Of two possible structures **10b** and **11b,** the former must be the correct one as no reasonable precursor for **11b** exists.



The formation of **10b** can be ascribed to initial photocyclization at C-2′ (reaction B) instead of C-6′ (reaction A, see eq 1). Subsequent elimination of hydrogen chloride, possibly



(1)

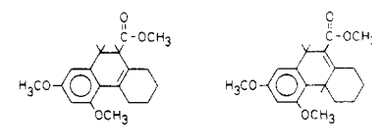
in the same way as reported for the comparable elimination of methanol in the photocyclization of 2-methoxystilbene, should then give **10b.**[6]

It is remarkable that **10b** is not found as a product in the oxidative photocyclization of **1b.** An explanation might be that the ratio **2b/12b** is high and the oxidation of **2b** more rapid. Under nonoxidative conditions the formation of hydrogen chloride (from **12b**) might interfere with the continuation of the process, promoting the formation of **10b** and considerable amounts of polymeric products.

To prevent any possible influence of the acid formed, the irradiation of **1b** was repeated under identical conditions, except for the presence of some powdered anhydrous potassium carbonate in the reaction medium. Three products were isolated in yields of 32, 16 and 2%, respectively. The mass spectrum of the major product gave a parent ion *m/e* 310, indicating a structure isomeric with the starting material. The IR spectrum showed an unconjugated ester carbonyl (1740 cm^{-1}). The NMR spectrum (220 MHz) contained a similar ABC pattern at slightly different δ values as found for **8a;** 3 doublets of doublets at δ 3.30 (J_{AC} = 6.6, J_{BC} = 4.7 Hz), 2.73 (J_{AB} = 14.6, J_{AC} = 6.6 Hz), and 3.33 (J_{AB} = 14.6 J_{BC} = 4.7 Hz). In the UV spectrum λ_{max} 274 nm (ε 7740) is comparable to values found for several 5,6,7,8,9,10-hexahydrophenanthrenes[6] (maxima around 268–275 and/or 277–280 nm, extinction coefficients from 10 000 to 19 000). The structure must, therefore, be **8b,** corresponding to the main product of the nonoxidative irradiation of **1a.** Apparently the main routes for the photocyclizations of **1a** and **1b** under nitrogen are equal when potassium carbonate is added in the irradiation of **1b.**

The second and third photoproducts from **1b** were, respectively, the monochlorotetrahydrophenanthrene **10b,** also formed in the absence of the base, and **3b,** formed under oxidative conditions.

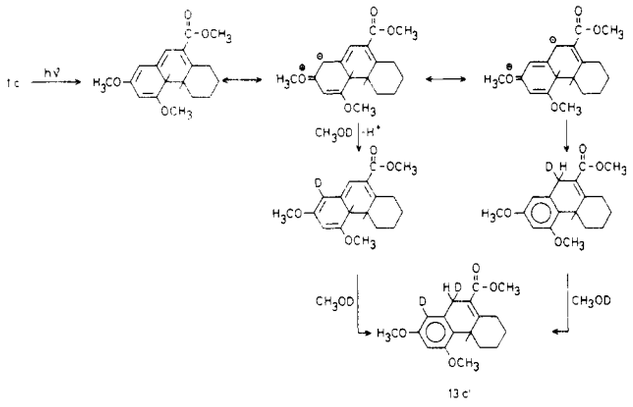
C. Methyl α-(1-cyclohexenyl)-3′,5′-dimethoxycinnamate (1c). On irradiation of **1c** in methanol under nitrogen, pure crystalline needles (mp 105–106 °C) precipitated from the ice–acetone-chilled reaction solution in 86.5% yield. The mass spectrum had the same parent peak as the starting material. The IR spectrum indicated a conjugated ester carbonyl (1710–1720 cm^{-1}), contrary to the expected structure **8c.**



Moreover, the UV spectrum showed λ_{max} 275 nm (ε 2080) and 283 (1910), the extinctions of which are considerably lower than that expected for a styrene chromophore. **13c** was the only reasonable structure that could be corroborated by the NMR spectrum (220 MHz), which showed the absence of vinyl protons, a broad two-proton singlet (δ 3.52) due to the methylene protons at C-10, a multiplet at δ 1.97 coupled to two other protons (J = 12, J' = 3.5 Hz) which can be ascribed to C-4b–H and a one-proton signal at δ 1.17 coupled to three adjacent protons (J = 24, J' = 12, J'' = 4 Hz) which can be ascribed to one of the protons at C-8, which is deshielded by the neighboring carbomethoxy group.

When the irradiation of **1c** was performed in perdeuter-

Scheme IV



iomethanol, **13c'**, containing two deuterium atoms, was isolated (Scheme IV). The integrated NMR spectrum of the deuterated product showed that the broad singlet (δ 3.52) had been reduced to a one-proton signal and that, in addition, one aromatic proton had been replaced. The same result was obtained on irradiation of **1c** in CH_3OD, indicating that the deuterium was introduced in an ionic process. It was established that deuterium exchange on the aromatic ring also occurred after the initial formation of **13c**. On irradiation of **13c** in $CDCl_3$ (or CH_3OD), the solution turned dark green (only in chloroform) and deuterium appeared in the aromatic ring, as shown by NMR (the same dark green solution occurred when **1c** was irradiated in chloroform). The exchange appears to be solely in one position, postulated to be the 1 position.

The incorporation of deuterium during the nonoxidative photocyclization of **1c** can be caused by the high electron density in the initially formed cyclization product **2c** as a consequence of the strongly electron-donating methoxy substituents. Subsequent reactions may be as shown in Scheme IV. It is not clear why the proton at C-3 does not exchange in a similar way.

It is remarkable that the shift of the second double bond in the central ring of the primary electrocyclization product (**2c**), which takes place in the photocyclization of **1a** and **1b**, fails to come about in the photolysis of **1c** under similar conditions.

Conclusion

In summary, it appears that on irradiation under oxidative conditions the α-(1-cyclohexenyl)cinnamic esters **1a–c** behave similarly as methyl α-phenylcinnamate; they are converted into the 5,6,7,8-tetrahydrophenanthrenes **3a–c** in high yields (Scheme II).

Under nonoxidative conditions, however, the primarily formed photoproducts (**2a–c**) undergo secondary reactions which strongly depend on the substituents present in the aromatic ring of the parent compound. With **1a** having a *p*-trifluoromethyl substituent, the process proceeds analogously to the photoconversion of the α-phenylcinnamic ester, as shown in Scheme I. In the photolysis of the dimethoxy compound (**1c**), however, the enolization step in Scheme I is surpassed by a very rapid ionic reaction as described in Scheme IV. The 2,4-dichloro derivative **1b** behaves differently as two isomeric primary photoproducts (**2b** and **12b**) arise. One of them, **12b**, spontaneously eliminates hydrochloric acid, which interferes with the formation of the "normal" product **8b**. Addition of potassium carbonate restores the formation of the latter product.

Experimental Section

All melting points were taken on a Thomas Hoover capillary melting point apparatus and are uncorrected. Elemental analyses were carried out either by Galbraith Laboratories, Inc., Knoxville, Tenn., or by the Schwarzkopf Microanalytical Laboratory, Woodside, N.Y.

The infrared (IR) spectra were recorded on a Perkin-Elmer Model 137 Infracord spectrophotometer. The ultraviolet (UV) spectra were taken with a Cary Model 14M recording spectrometer. All extinction coefficients are molar, the units being $cm^2\ mol^{-1}$. Nuclear magnetic resonance (NMR) spectra were recorded with either a (a) JEOL (Japan Electron Optics Laboratory Co.) Model JNM-MN-60, or (b) by Union Carbide Corp., Eastview, N.Y., on a Bruker 90-MHz instrument, or (c) by Rockefeller University's Nuclear Magnetic Resonance Laboratory on a Varian 220-MHz machine. In all proton magnetic resonance (NMR) spectra, tetramethylsilane was the internal reference. In the carbon-13 magnetic resonance (^{13}C NMR) spectra, perfluorobenzene was the reference. Mass spectra were determined on a Hitachi Perkin-Elmer RMS-4 mass spectrometer.

All chemical solvents were of reagent quality and were used as obtained from the manufacturers.

Irradiation solutions were placed in cylindrical quartz tubes (unless otherwise noted) of varying capacities. All tubes were approximately 30 cm long, but the diameters varied from 0.7 cm (6–7-mL capacity) to 2.3 cm (100-mL). The tubes were sealed by means of rubber serum caps and were then suspended in the center of a Rayonet–Srinivasan–Griffin photochemical reactor equipped with 16 300-nm lamps (21 W). The solution temperatures were typically 35–40 °C inside the reactor due to the heat generated by the lamps.

α-(1-Cyclohexenyl)-2',4'-dichlorocinnamic Acid (6b). To 15 mL of acetic anhydride in a 500-mL three-neck flask equipped with a mechanically driven stirring blade (Teflon), an addition funnel with a gas inlet adapter, and a condenser with a calcium chloride drying tube was added with stirring 2.5 g of dry sodium methoxide powder. The solution was externally heated to approximately 50 °C for 15 min. To this warm solution was added 6.0 g of melted 1-cyclohexenylacetic acid. The solution was heated at 50 °C for an additional 30 min, during which time "swelling and coagulation" occurred, which necessitated efficient stirring and heating to maintain a homogeneous liquid phase. To the still warm solution 5.0 g of 2,4-dichlorobenzaldehyde without any additional washing was added. The solution was heated to 110 °C overnight.

The solution, still warm, was treated with 5-mL portions of water over a 2-h period while stirring and heating was continued. Approximately 60–75 mL of water was used altogether. Precipitation occurred more efficiently and faster recovery of the acid was achieved by taking up the entire oily solid directly into diethyl ether in a separatory funnel and washing with water until the washings were neutral. The ethereal layer was washed twice with sodium bicarbonate solution and then with water again (the smaller molecular weight 2,4-dichlorocinnamic acid, mp 232–233 °C, a byproduct of the condensation of the aldehyde with acetic anhydride, appeared to be removed in the bicarbonate wash. Excessive base washings could cause loss of the desired acid). The ether layer was then washed with saturated sodium bisulfite solution to remove any unreacted aldehyde and then with water. After drying over magnesium sulfate and filtering, the solvent was evaporated on a rotary evaporator. Recrystallization of the crude solid in boiling carbon tetrachloride removed the remaining cinnamic acid, 0.4 g, mp 230–232 °C. Further recrystallization from hexane gave 4.3 g of the desired acid (50.5%), mp 141–150 °C (probably a mixture of the cis and trans isomers), as cream-colored needles. The IR spectrum (KBr pellet) gave ν_{max} 2900, 2600, 1680, 1580, 1470, 1415, 1280, 1100, 1050, 925, 870, 825, 815, and 783 cm^{-1}. The NMR spectrum (CD_3OD) showed peaks at δ 7.3–7.7 (4 H, m), 5.5 (1 H, brd s), and 2.1 and 1.7 (8 H, converging m). The mass spectrum gave parent ion *m/e* 296 and indicated the presence of two chlorines.

Anal. Calcd for $C_{15}H_{14}Cl_2O_2$: C, 60.60; H, 4.75; Cl, 23.90. Found: C, 60.06; H, 4.72; Cl, 25.15.

α-(1-Cyclohexenyl)-4'-trifluoromethylcinnamic Acid (6a). The same general method was used as in the preparation of **6b**. Recrystallization from a minimum amount of boiling CCl_4 removed 0.2 g of the cinnamic acid byproduct, mp 229–230 °C. Chilling of the mother liquor in dry ice/acetone gave 4.4 g of the desired acid, mp 122–129 °C. The IR spectrum (KBr pellet) gave ν_{max} 2900, 1685, 1620, 1416, 1322, 1280, 1165, 1132, 1070, and 1017 cm^{-1} (the cinnamic acid byproduct gave ν_{max} 2300–3300, 1685, 1640, 1430, 1320, 1290, 1225, 1180, 1140, 1075, 1020, 990, 840, and 700 cm^{-1}). The NMR spectrum ($CDCl_3$) showed signals at δ 1.57–2.45 (8 H, m), 6.01 (1 H, brd s), and 8.13 (5 H, s). The mass spectrum gave parent ion *m/e* 296.

Anal. Calcd for $C_{16}H_{15}F_3O_2$: C, 64.86; H, 5.10; F, 19.24. Found: C, 65.07; H, 4.95; F, 17.89. Anal. Calcd for the cinnamic acid byproduct $C_{10}H_7F_3O_2$: C, 55.56; H, 3.27; F, 26.37. Found: C, 55.92; H, 3.46; F, 24.94.

α-(1-Cyclohexenyl)-3′,5′-dimethoxycinnamic Acid (6c). The same method was used as in the preparation of 2,4-dichloro- and 4-trifluoromethyl derivatives. Quantities of reagents used were acetic anhydride, 20 mL (total), sodium methoxide, 3.2 g (total), cyclohexenylacetic acid, 7.0 g, and 3,5-dimethoxybenzaldehyde, 8.3 g. Workup was simplified since the acid could be filtered from the aqueous acidified solution. Total yield was 10.5 g (73%), mp 121.5–133.5 °C. The IR spectrum (KBr pellet) gave ν_{max} 2900, 1675, 1590, 1457, 1422, 1341, 1280, 1208, 1160, 1072, and 1060 (doublet), 925, 873, and 831 cm^{-1}. The NMR spectrum (CCl_4) showed δ 1.85 and 2.25 (8 H, brd m) and singlets at δ 4.08 (6 H), 6.17 (1 H, brd), 6.81 (1 H, brd), 7.26 (1 H), 732 (1 H), and 8.17 (1 H). The mass spectrum gave parent *m/e* 288.

Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.81, 70.62; H, 6.96, 7.11.

Methyl α-(1-Cyclohexenyl)-2′,4′-dichlorocinnamate (1b). A solution of 0.4 g of the acid in 15 mL of absolute methanol containing 0.75 mL of concentrated H_2SO_4 was refluxed for 2 h, after which it was cooled to room temperature and allowed to stand over the weekend. The solution was poured onto crushed ice and extracted with diethyl ether. The ether extracts were washed with a saturated $NaHCO_3$ solution until the rinsings were basic and then with water. After drying over Na_2SO_4 and filtering, evaporation of the solvent gave 0.5 g (100%) of the crude ester as an oil.

The IR spectrum (liquid film) gave ν_{max} 2900, 2820, 1710, 1580, 1455, and 1430 (doublet), 1380, 1245, 1145, 1100, 1050, 1025, 930, 870, 818, 790, 767, and 748 cm^{-1}. The NMR spectrum (CCl_4) showed two converging multiplets centered at δ 1.6 and 2.0 (8 H) and signals at δ 3.75 (3 H, s), 5.47 (1 H, brd s), and 7.0–7.6 (4 H, m). The mass spectrum showed parent ion *m/e* 310 and indicated the presence of two chlorines.

Anal. Calcd for $C_{16}H_{16}Cl_2O_2$: C, 61.73; H, 5.18; Cl, 22.81. Found: C, 61.85; H, 5.12; Cl, 23.20.

Methyl α-(1-Cyclophexenyl)-4′-trifluoromethylcinnamate (1a). Mp 66–70 °C. The IR spectrum (KBr pellet) gave ν_{max} 3400, 2930, 1720, 1620, 1440, 1330, 1243, 1212, 1170, 1133, 1073, 1022, 946, 926, 854, 839, 744, and 722 cm^{-1}. The NMR spectrum (CCl_4) gave δ 1.4–2.4 (8 H, m), 3.95 (3 H, s), 5.88 (1 H, brd s), 7.90 (1 H, s), and 8.10 (4 H). The mass spectrum showed a parent ion at *m/e* 310.

Anal. Calcd for $C_{17}H_{17}F_3O_2$: C, 65.80; H, 5.52; F, 18.69. Found: C, 65.47; H, 5.37; F, 21.08.

Methyl α-(1-Cyclohexenyl)-3′,5′-dimethoxycinnamate (1c). The IR spectrum (smear) gave ν_{max} 2900, 1710, 1585, 1452 and 1425 (doublet), 1230, 1156, 1069, 1020, 922, and 837 cm^{-1}. The NMR spectrum (CCl_4) gave δ 1.85 and 2.34 (8 H, brd m), 4.08 (9 H, s), 6.08 (1 H, brd s), 6.88 (1 H, t, J = 2.3 Hz), 7.30 (2 H, d, J = 2.3 Hz), and 8.04 (1 H, s). The mass spectrum gave parent ion *m/e* 302.

Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.44; H, 7.34. Found: C, 71.38; H, 7.29.

Methyl 1,3-Dichloro-5,6,7,8-tetrahydrophenanthrene-9-carboxylate (3b) from the Oxidative Irradiation of Methyl α-(1-Cyclohexenyl)-2′,4′-dichlorocinnamate (1b). A solution of 1.0 g of the methyl cinnamate in 100 mL of absolute methanol containing 0.5 g of iodine was irradiated for 15 h. The product crystallized out of the cooled solution. Filtration and washing with hexane gave 0.4 g of the tetrahydrophenanthrene **3b,** mp 127–128 °C, as colorless needles. (This product can also be recrystallized from hexane/ether or sublimed below its melting point at 80–100 mm.) More product, 0.2 g, was recovered from the mother liquor by chromatographing the concentrated oil on silica gel and eluting with 1:1 hexane/benzene. Total yield was 0.6 g (61.7%). The IR spectrum (KBr pellet) gave ν_{max} 2900, 1710, 1602 and 1575 (doublet), 1425, 1260, 1180, 1153, 1090, 1030, 1008, 900, 861, 802, and 779 cm^{-1}. The NMR spectrum (CCl_4) gave peaks at δ 1.75 and 2.95 (8 H, m), 3.80 (3 H, s), and three one-proton singlets at δ 7.3, 7.6, and 8.25. The mass spectrum showed parent ion *m/e* 308. The UV spectrum (MeOH) showed λ_{max} 344 nm (ε 2650), λ_{sh} 332 (2720), and λ_{max} 292–300 flat (11 370).

Anal. Calcd for $C_{16}H_{14}Cl_2O_2$: C, 62.13; H, 4.56; Cl, 23.28. Found: C, 61.66; H, 4.61; Cl, 25.32.

Methyl 3-Trifluoromethyl-5,6,7,8-tetrahydrophenanthrene-9-carboxylate (3a) from the Oxidative Irradiation of Methyl α-(1-Cyclohexenyl)-4′-trifluoromethylcinnamate (1a). Yield 71%, mp 64–64.5 °C. The IR spectrum (KBr pellet) showed ν_{max} 2900, 1735, 1437, 1380, 1323, 1300, 1178, 1155, 1140, 1075, 999, and 905 cm^{-1}. The NMR spectrum ($CDCl_3$) showed signals at δ 2.06 (4 H, m), 3.39 (4 H, m), 4.28 (3 H, s), 8.29 (1 H, d J = 9 Hz), 8.59 (1 H, d, J = 9 Hz), 8.88 (1 H, s), and 9.00 (1 H, s). The mass spectrum gave parent ion *m/e* 308.

Anal. Calcd for $C_{17}H_{15}F_3O_2$: C, 66.23; H, 4.90; F, 18.49. Found: C, 66.57; H, 4.95; F, 17.94.

Methyl 2,4-Dimethoxy-5,6,7,8-tetrahydrophenanthrene-9-carboxylate (3c) from the Oxidative Irradiation of Methyl α-(1-Cyclohexenyl)-3′,5′-dimethoxycinnamate (1c). Yield 65.0%, mp 89–91 °C. The IR spectrum (CCl_4) showed ν_{max} 2900, 1730, 1625, 1452, 1390, 1310, 1260, 1203, 1153, 1067, 1020, and 950 cm^{-1}. The NMR spectrum ($CDCl_3$) showed broad multiplets at δ 1.6–2.1 (4 H) and 3.0–3.9 (4 H). Two poorly separated singlets appeared at δ 3.96 (6 H) and 4.00 (3 H) and other peaks at δ 4.1 (3 H, s), 6.79 (1 H, d, J = 2.5 Hz), 6.99 (1 H, d, J = 2.5 Hz), and 8.35 (1 H, s). The mass spectrum gave a parent ion *m/e* 300.

Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.88; H, 6.79.

Methyl 3-Chloro-5,6,7,8-tetrahydrophenanthrene-9-carboxylate (10b) from the Nonoxidative Irradiation of Methyl α-(1-Cyclohexenyl)-2′,4′-dichlorocinnamate (1b). A solution of 2.5 g of the acrylate in 1000 mL of absolute methanol was placed in a large quartz vessel and purged for 30 min with a stream of dry nitrogen. The solution was irradiated for a total of 102 h and checked at 71, 96, and 102 h, respectively, by thin-layer chromatography (silica gel sheets developed in 9:2 hexane/diethyl ether) until little or no starting material was observed (starting material had an R_f 0.43 and absorbed 2537-Å light, while the product had R_f 0.36 and fluoresced in 2537-Å light). An NMR sampling of the final reaction solution showed less than 10% starting ester remaining.

The entire solution was evaporated to a semisolid residue, which was taken up in diethyl ether and dried over Na_2SO_4. After filtration and evaporation, 2.8 g of an oily brownish yellow residue was obtained. This oil was chromatographed on silica gel, eluting with 25% diethyl ether in hexane, to give 0.5 g of solid, mp 78–98 °C, and 0.1 g of solid, mp 82–94 °C. Recrystallization from methanol/hexane removed starting material and left a fairly pure product in the mother liquor. The recovery of product (mp 96–104 °C) of reasonable purity was 34.1%, 0.6 g. The IR spectrum (liquid film) gave ν_{max} 2900, 2820, 1720, 1620, 1585, 1440, 1365, 1280, 1237, 1205, 1150, 1080, 1025, 997, 902, 874, and 805 cm^{-1}. The mass spectrum showed parent ion *m/e* 274, with major fragments at 242, 214, 195, and 197. Only one chlorine was indicated. The NMR spectrum (CCl_4, 220 MHz) showed signals at δ 7.26 (1 H, dd, J = 9, J' = 1.5 Hz), 7.57 (1 H, d, J = 9 Hz), 7.76 (1 H, d, J = 1.5 Hz), 7.98 (1 H, s), 3.85 (3 H, s), 3.05 (2 H, t, J = 6 Hz), 2.95 (2 H, t, J = 6 Hz), and 1.73 (4 H, m). The 60-MHz spectrum (CCl_4) showed δ 1.93 (6 H, m), 3.25 (4 H, m), 3.95 (3 H, s), and 7.45–8.40 (4 H, m). The UV spectrum (MeOH) showed λ_{sh} 340 nm (ε 3330) and λ_{max} 301 (4420), 280–290 flat (6750), and 241 (48 000).

Anal. Calcd for $C_{16}H_{15}ClO_2$: C, 69.94; H, 5.50; Cl, 12.91. Found: C, 69.88; H, 5.51; Cl, 12.42.

Methyl 1,3-Dichloro-5,6,7,8,9,10-hexahydrophenanthrene-9-carboxylate (8b) from the Nonoxidative Irradiation of Methyl α-(1-Cyclohexenyl)-2′,4′-dichlorocinnamate (1b) in the Presence of Potassium Carbonate. A solution of 1.0 g (3.2×10^{-3} M) of cinnamate **1b** dissolved in 75 mL of absolute methanol containing 0.4 g (3.2×10^{-3} M) of potassium carbonate was purged with a gentle stream of nitrogen for 30 min and then irradiated for 15 h. The solution was poured into 50 mL of diethyl ether and extracted with 25-mL portions of aqueous saturated salt solution until the washings were neutral. After drying over $MgSO_4$ and filtering, evaporation of the ether gave 0.9 g of a yellowish oily residue. The residue was chromatographed on a 12 × 0.44 in. o.d. column of silica gel, eluting with increasing amounts of chloroform in pentane (10–100%). Based on NMR integrations of the eluted fractions, 0.18 g of starting material was recovered. The three products were methyl 1,3-dichloro-5,6,7,8,9,10-hexahydrophenanthrene-9-carboxylate (**8b**), 0.27 g (32.4%), methyl 3-chloro-5,6,7,8-tetrahydrophenanthrene-9-carboxylate (**10b**), 0.12 g (15.7%), and methyl 1,3-dichloro-5,6,7,8-tetrahydrophenanthrene-9-carboxylate (**3b**), 0.02 g (1.8%). The structures of the two tetrahydrophenanthrenes were established by comparison with authentic materials.

Repetitive column chromatography gave 0.09 g of pure hexahydro product **8b** as an oil. The IR spectrum (CCl_4) gave ν_{max} 2905, 1740, 1580–1540, 1455 and 1440 (doublet), 1170–1160, 1098, 1090, 1028, and 860 cm^{-1}. The NMR spectrum (CCl_4, 220 MHz) gave δ 1.74 (4 H, m), 2.31 (4 H, m), 2.73 (1 H, dd, J_{AB} = 14.6, J_{AC} = 6.6 Hz), 3.30 (1 H, dd, J_{AC} = 6.6, J_{BC} = 4.7 Hz), 3.33 (1 H, dd, J_{AB} = 14.6, J_{BC} = 4.7 Hz), 3.56 (3 H, s), and an AB quartet at δ 6.93 and 7.04 (2 H, J = 2.00 Hz). The mass spectrum showed parent ion *m/e* 310, with a base peak of 251. Other major fragments were 211, 209, 191, and 189. Two chlorines were indicated. The UV spectrum (MeOH) had λ_{max} 274 nm (ε 7740), 249 (10 760), 237 (18 410), 230 (21 360), and 224 (20 590).

Anal. Calcd for $C_{16}H_{16}Cl_2O_2$: C, 61.75; H, 5.18; Cl, 22.79. Found: C, 61.73; H, 5.09.

Attempts to oxidize the hexahydrophenanthrene system to either

the tetrahydrophenanthrene or the phenanthrene using Pd- or Pt-on-carbon or *N*-bromosuccinimide and dibenzoyl peroxide gave no reaction.

Methyl 3-Trifluoromethyl-5,6,7,8,9,10-hexahydrophenanthrene-9-carboxylate (8a) from the Nonoxidative Irradiation of Methyl α-(1-Cyclohexenyl)-4′-trifluoromethylcinnamate (1a). A solution of 0.50 g of cinnamate **1a** in 50 mL of absolute methanol containing 0.122 g of K_2CO_3 was purged with nitrogen and irradiated for 15 h. The solution was taken up in diethyl ether, washed with water, dried over $MgSO_4$, filtered, and evaporated to give 0.54 g of a yellow oil. The oil was taken up in chloroform and chromatographed on a 12 × 0.5 in. column of silica gel, eluting with increasing amounts of chloroform in hexane (10–100%). The products were methyl 3-trifluoromethyl-5,6,7,8-tetrahydrophenanthrene-9-carboxylate (**3a**), 0.02 g (4.6%), methyl 3-trifluoromethyl-5,6,7,8,9,10-hexahydrophenanthrene-9-carboxylate (**8a**), 0.29 g (57.0%), and 4-trifluoromethyl-5,6,7,8,9,10-hexahydrophenanthrene-9-carboxylic acid (**9a**), mp 154–161 °C dec, 0.11 g (23.9%). The IR spectrum (smear) of **8a** showed ν_{max} 2900, 1745, 1432, 1330, 1278, 1243, 1165, 1120, 1098, 1080, 990, 895, and 841 cm^{-1}. The NMR spectrum (CCl_4, 60 MHz) showed signals at δ 1.99 (4 H, m), 2.6 (4 H, brd m), 3.4 (3 H, m) 3.95 (3 H, s), and 8.12 (3 H, m). A 220-MHz (CCl_4) scan showed δ 0.88 (1 H, q, J = 6 Hz), 1.27 (1 H, s), 1.78 (2 H, m), 1.90 (1 H, m), 2.16 (1 H, m), 2.39 (1 H, m), 2.60 (1 H, m), 2.95 (1 H, dd, J = 6, J' = 13–13.5 Hz), 3.57 (3 H, s), 7.17 (1 H, d, J = 6.8–7 Hz), 7.34 (1 H, d, J = 6.8–7 Hz), and 7.37 (1 H, s). UV and analytical data were obtained on the solid acid derivative **9a** (see below).

3-Trifluoromethyl-5,6,7,8,9,10-hexahydrophenanthrene-9-carboxylic Acid (9a) from the Hydrolysis of Methyl 3-Trifluoromethyl-5,6,7,8,9,10-hexahydrophenanthrene-9-carboxylate (8a). A solution of 0.20 g of the hexahydrophenanthrene methyl ester (**8a**) in 10 mL of absolute methanol containing 20 mL of 25% aqueous sodium hydroxide was refluxed overnight. The basic solution was cooled and extracted with diethyl ether. The aqueous layer was acidified with HCl and extracted with ether. After drying over $MgSO_4$, the solution was filtered and evaporated to give 0.16 g (81.4%) of a white powder, mp 162.5–163.5 °C dec [sublimes ~150 °C (760 mm)].

This material was identical with that obtained in the irradiation above. The IR spectrum (KBr pellet) showed ν_{max} 3350, 3050, 2900, 2700–2500, 1710, 1415, 1333, 1273, 1236, 1167, 1120, and 840 cm^{-1}. The NMR spectrum (CCl_4, 220 MHz) gave δ 1.59–2.05 (4 H, m), 2.05–2.73 (4 H, m), 2.98 (1 H, dd, J = 20, J' = 6.5–7 Hz), 2.99 (1 H, s), 3.17 (1 H, dd, J = 20, J' = 8 Hz), 7.14 (1 H, d, J = 8 Hz), 7.30 (1 H, d, J = 8 Hz), 7.35 (1 H, s), and 11.23 (1 H, brd s). The mass spectrum gave parent ion m/e 296. The UV spectrum (MeOH) gave λ_{max} 275 nm (ε 5760) and 225 (12 660).

Anal. Calcd for $C_{16}H_{15}F_3O_2$: C, 64.86; H, 5.10; F, 19.24. Found: C, 64.57; H, 4.88; F, 18.75.

Irradiation of Methyl α-(1-Cyclohexenyl)-4′-trifluoromethylcinnamate (1a) using a Pyrex Filter. A solution containing 0.9 g of **1a** in 90 mL of absolute methanol was purged for 1 h with a stream of dry nitrogen and placed in a Pyrex tube. After irradiating for 15 h, the solvent was removed on a rotary evaporator to give 0.9 g of a yellow oil. The NMR of this oil indicated only starting ester.

The recovered **1a** from the above irradiation was dissolved in 90 mL of absolute methanol containing 0.4 g of K_2CO_3. After purging for 1 h with nitrogen and irradiating for 15 h, the solvent was removed to give 0.9 g of unreacted **1a**.

Nonoxidative Irradiation of Methyl α-(1-Cyclohexenyl)-4′-trifluoromethylcinnamate (1a) in Perdeuteriomethanol. A solution of 0.3 g of the ester in 15 mL of CD_3OD was purged with nitrogen and irradiated (quartz) for 25 h. An NMR spectrum of the crude reaction residue, after solvent removal, showed mostly unreacted ester. The residue was redissolved in 15 mL of CD_3OD with 0.05 g of K_2CO_3 in it, repurged, and irradiated for an additional 20 h. Workup, followed by drying over $MgSO_4$ and filtering, gave 0.3 g of a yellow oil (NMR showed little or no starting material remaining). This was chromatographed over silica gel, eluting with hexane followed by 10% $CHCl_3$ in hexane. Of 50–75-mL fractions, fractions 33–38 contained 0.1 g of impure **3a**. Fractions 39–41 gave 0.14 g of partially deuterated **8a** (see text for discussion of NMR spectrum).

Methyl Dimethoxy-5,5α,6,7,8,10-hexahydrophenanthrene-9-carboxylate (13c) from the Nonoxidative Irradiation of Methyl α-(1-Cyclohexenyl)-3′,5′-dimethoxycinnamate (1c). A solution of 1.0 g of cinnamate **1c** in 100 mL of absolute methanol was purged for 1 h with nitrogen. After irradiating for 15 h, the reaction was cooled in an ice/acetone bath to induce crystallization of the product. Filtering, washing sparingly with chilled 1:1 MeOH/H_2O, and air-drying gave 0.87 g of colorless needles (86.5%), mp 105–106.5 °C. The IR spectrum (CCl_4) showed ν_{max} 2900, 1720, 1600, 1492, 1460, 1428, 1380, 1343, 1270, 1240, 1200, 1155, 1120, 1099, and 1060 cm^{-1}. The NMR spectrum showed a marked solvent effect; therefore, results obtained with both CCl_4 and C_6D_6 (220 MHz) are reported here. NMR (C_6D_6) δ 1.32 (1 H, octet, J_1 = 23.5, J_2 = 12, J_3 = 5 Hz), 1.48–1.70 (3 H, m), 1.73–1.93 (2 H, m), 2.55 (1 H, multiplet of doublets, J = 12–12.5 Hz), 3.27 (3 H, s), 3.39 (3 H, s), 3.47 (3 H, s), 3.58 (1 H, q of d, J_1 = 10.5–11, J_2 = 7, J_3 = 3.75 Hz), 3.74 (2 H, d, J = 3 Hz), 4.02 (1 H, m of d, J = 10.5–11 Hz), 6.17 (1 H, d, J = 2.3 Hz), and 6.31 (1 H, d, J = 2.3 Hz). NMR (CCl_4) δ 1.17 (1 H, octet, J_1 ~ 24, J_2 ~ 11.5–12, J_3 ~ 4 Hz), 1.36–1.6 (1 H, m), 1.6–1.9 (3 H, m), 1.97 (1 H, brd d with fine structure, J ~ 12 Hz), 2.30 (1 H, ibid.), 3.35 (1 H, m), 3.52 (2 H, brd s), 3.6–3.7 (1 H, m), 3.67 (6 H, s), 3.76 (3 H, s), and 6.12 (2 H, AB q, J = 2.5). A carbon-13 NMR spectrum (CCl_4, 22.63 MHz) was obtained in a effort to verify the presence of the tetrasubstituted internal double bond, and it was found to be entirely consistent with the proposed structure. Bands are reported in ppm (from Me_4Si) (one carbon unless noted otherwise): 28.2, 31.2, 32.8, 33.8, 38.1, 42.2, 51.8, 55.9 (2 C), 103.1, ~132.4 (buried under C_6F_6 internal standard), 118.4 (2 C), 135.0, 153.3, 158.4, 160.0, and 168.3 ppm. The UV spectrum (MeOH) gave λ_{max} 283 nm (ε 1910), 275 (2080), and strong end absorption. The mass spectrum showed parent ion m/e 302. The molecular weight by the Rast method was found to be 300.

Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.34. Found: C, 71.29; H, 7.48.

Attempted Rearrangement of Methyl 2,4-Dimethoxy-5,5α,6,7,8,10-hexahydrophenanthrene-9-carboxylate (13c) to Methyl 2,4-Dimethoxy-5,6,7,8,9,10-hexahydrophenanthrene-9-carboxylate (8c). A solution of 0.1 g of hexahydrophenanthrene **13c** dissolved in 15 mL of benzene containing 0.05 g of *p*-toluenesulfonic acid (monobasic) was refluxed overnight. The reaction solution was washed with saturated aqueous sodium bicarbonate solution and water, dried over Na_2SO_4, filtered, and evaporated to give 0.1 g of unreacted starting material (IR, NMR).

Attempted Oxidation of Methyl 2,4-Dimethoxy-5,5α,6,7,8,10-hexahydrophenanthrene-9-carboxylate (13c) to Methyl 2,4-Dimethoxy-5,6,7,8-tetrahydrophenanthrene-9-carboxylate (3c) or Its Phenanthrene Derivative. Method A. Powdered 10% palladium-on-carbon, 0.15–0.20 g, was added to 0.25 g of the hexahydro compound **13c** in 10 mL of xylene. The solution was refluxed for 70 h. After cooling, filtering, and removing the xylene by distillation, the residue was shown to be only starting material (IR, TLC).

Method B. A mixture of 0.15 g of the hexahydrophenanthrene **13c**, 0.16 g of *N*-bromosuccinimide, 0.03 g of dibenzoyl peroxide, 0.7 g of potassium acetate, and 0.87 mL of glacial acetic acid in 6.5 mL of carbon tetrachloride was maintained at reflux for 16 h, during which time additional quantities of dibenzoyl peroxide were added. (The presence of an orange solution indicated that additional peroxide was necessary.) The cooled solution was poured into cold 5% aqueous HCl, and the precipitate was collected and washed well with water and a small amount of benzene. The IR spectrum indicated only unreacted starting material.

Method C. A solution of 0.11 g of **13c** and 0.03 g of the biacetyl in 20 mL of benzene was irradiated over the weekend with 3500-Å light. After solvent removal, the residue was extracted with benzene and washed with water. The solution was passed through 2 g of alumina, eluting with light petroleum ether/benzene (1:1). A complete recovery or unreacted starting material was obtained.

Methyl 2,4-Dimethoxy-5,5α,6,7,8,10-hexahydro-1,10-dideuteriophenanthrene-9-carboxylate (13c′) from the Nonoxidative Irradiation of Methyl α-(1-Cyclohexenyl)-3′,5′-dimethoxycinnamate (1c) in Deuteriomethanol. A solution containing 0.6 g of cinnamate **1c** and 0.28 g of K_2CO_3 in 25 mL of CD_3OD was purged for 1 h with nitrogen and irradiated for 30 h (after 15 h, 20% of the starting cinnamate was still present). The solvent was removed, and the yellow oily residue was taken up in diethyl ether and washed with D_2O. After drying over $MgSO_4$ and filtering, the ether was removed to give 0.6 g of yellow oil (crude NMR indicated little or no starting material or tetrahydrophenanthrene **3c**), which was chromatographed on silica gel, eluting with increasing amounts of chloroform in hexane. The first fractions gave a yellow–brown crystalline product, 0.28 g (46%), mp 99.5–102 °C, which could be further purified to a colorless powder by recrystallization from CCl_4, mp 101–103 °C (the spectral data were obtained on this sample). Further elutions gave 0.34 g (55%) of a yellow viscous oil, the NMR and IR of which indicate that the material is essentially the same structure as above, except that it may be a mixture of differently deuterated materials. The IR spectrum (KBr pellet) gave weak CD bands at ν_{max} 2075 and 2220 cm^{-1}. The relative intensity of the CH bands (relative to C=O) was

considerably lower than in the undeuterated material. The carbonyl band was unchanged (1710 cm^{-1}) while other significant bands fell at 1600, 1460, 1425, 1363, 1340, 1222, 1122, and 837 cm^{-1}. (See text for a discussion of the NMR spectrum.) The mass spectrum gave parent ion *m/e* 304 and indicated the absence of any oxidative product or material that was deuterated additionally.

Irradiation of **1c** under identical conditions in monodeuteriomethanol (CH_3OD) yielded **13c'** also.

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Registry No.—**1a**, 64490-61-5; **1b**, 64490-62-6; **1c**, 64490-63-7; **3a**, 64490-64-8; **3b**, 64490-65-9; **3c**, 64490-66-0; **4a**, 455-19-6; **4b**, 874-42-0; **4c**, 7311-34-4; **5**, 18294-87-6; **6a**, 64490-67-1; *E*-**6b**, 64490-68-2; *Z*-**6b**, 64490-69-3; **6c**, 64490-70-6; **7a**, 2062-26-2; **7b**, 1201-99-6; **8a**, 64490-71-7; **8b**, 64490-72-8; **9a**, 64490-73-9; **10b**, 64490-74-0; **13c**, 64490-75-1; **13c'**, 64490-76-2.

References and Notes

(1) (a) M. V. Sargent and C. J. Timmons, *J. Chem. Soc.*, 5544 (1964); (b) G. Rio and J. C. Hardy, *Bull. Soc. Chim. Fr.*, 3578 (1970); (c) K. Ichimura and S. Watanabe, *Bull. Chem. Soc. Jpn.*, **49**, 2224 (1976); (d) R. Srinivasan and J. N. C. Hsu, *J. Am. Chem. Soc.*, **93**, 2816 (1971).
(2) P. H. C. op het Veld and W. H. Laarhoven, *J. Am. Chem. Soc.*, **99**, 7221, (1977).
(3) R. J. Hayward and C. C. Leznoff, *Tetrahedron*, **27**, 2085 (1971).
(4) A. Santiago and R. S. Becker, *J. Am. Chem. Soc.*, **90**, 3654 (1968).
(5) F. Toda and Y. Todo, *J. Chem. Soc., Chem. Commun.*, 848 (1976).
(6) R. G. F. Giles and M. V. Sargent, *J. Chem. Soc., Chem. Commun.*, 215 (1974).
(7) (a) P. N. Rao, E. J. Jacob, and L. R. Axelrod, *J. Chem. Soc. C*, 2855 (1971); (b) P. N. Rao and L. R. Axelrod, *ibid.*, 2861 (1971); (c) P. N. Rao, B. E. Edwards, and L. R. Axelrod, *ibid.*, 2863 (1971); (d) P. A. Robins and J. Walker, *J. Chem. Soc.*, 3249 (1956); (e) Z. G. Hajos, K. J. Doebel, and M. W. Goldberg, *J. Org. Chem.*, **29**, 2527 (1964); (f) Z. G. Hajos, D. R. Parrish, and M. W. Goldberg, *ibid.*, **30**, 1213 (1965); (g) J. Heer and K. Mieschler, *Helv. Chim. Acta*, **31**, 219 (1948); (h) R. B. Woodward and R. H. Eastman, *J. Am. Chem. Soc.*, **66**, 674 (1944); (i) J. A. Hogg, *ibid.*, **71**, 1918 (1949); (j) R. E. Juday, *ibid.*, **75**, 3008 (1953).

Synthetic Studies on Lignan Lactones: Aryl Dithiane Route to (±)-Podorhizol[1] and (±)-Isopodophyllotoxone and Approaches to the Stegane Skeleton

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The details of the conjugate addition of aryl dithiane anions to 2-butenolide are discussed. The results of the trapping of the resultant lactone enolates with an aryl halide and aryl aldehyde are detailed. The transformation of these intermediates into podorhizol (**4a**) and isopodophyllotoxone (**12a**) is also explored. The structures of products from attempted intramolecular Ullmann couplings in the stegnane series are established.

The antileukemic lignan lactones steganacin (**1a**) and steganangin (**1b**)[4] are but only two members of a growing class of naturally occurring bis(benzyl)[*a,c*]cyclooctadienes which include among their members schizandrin,[5] kadsurin, kadsuranin,[6] and gomisins A, B (**2a**), C (**2b**),[7] and D (**2c**).[8] The unusual ring system present in these substances and the close biogenetic relationship between the structures **1** and the antitumor lactone podophyllotoxin[9] **3** and its derivatives[10] have both initiated and renewed interest in the development of new methodology for the synthesis of these substances. To date the syntheses of steganacin,[11] steganone,[11,12] isostegane,[13] and deoxyschizandrin[14] have been realized.

Our concern in this area lay in the development of an efficient synthetic method which would be amenable to the construction of members of the stegane, podophyllane, and secopodophyllane (e.g., podorhizol (**4a**)) families. It appeared attractive to employ an acyl anion equivalent of piperonal which could undergo conjugate addition to 2-butenolide and whose resultant lactone anion could effect subsequent alkylation or aldol condensation with the appropriate benzylic halide or aromatic aldehyde (Scheme I).

Although the anions **5a–d** failed to give clean addition products, the thioethyl acetal anion provided the Michael adduct **7a** in 50% yield when exposed to 2-butenolide in THF at −78 °C[15] followed by low-temperature protonation. This yield was measurably improved (88%) by employing the dithiane **5f**, thereby providing the congener **7b**. Anion **5f** and the dithiane anion of benzaldehyde both added in a conjugate fashion to methyl cinnamate and methyl crotonate in 70–85% yield. The lactone enolate of **7b** could be generated successfully with lithium diisopropylamide (LDA) in THF at −78 °C followed by alkylation (−78 → 25 °C) with 3,4,5 trimethoxybenzyl chloride in the presence of 1 equiv of hexamethylphosphoramide (HMPA) in 56% yield. A more efficient route involved the direct alkylation[17] of the lactone enolate generated by Michael addition, thereby providing all of the required carbon atoms present in these lactones in a one-pot reaction. It was assumed at this point that the stereochemistry of **6a** was trans since it would be expected that alkylation would occur trans to the bulky aryl dithiane moiety. The assignment was confirmed when the dithiane was cleaved with HgO–BF_3 in aqueous THF to provide the ketone **6d**, prepared by Drake[18] some 20 years earlier. Moreover, the dithiane **6a** was transformed as described by Schlessinger[13] (Ni(R); VOF_3) to isostegane (**8**), whose unnatural biphenyl twist and trans-fused lactone have been defined by x-ray analysis. Any conversion of isostegane (**8**) to steganone (**1c**) would be dependent upon a selective benzylic oxidation to introduce oxygen and relieve the unnatural biphenyl twist.[19]

The intramolecular oxidative coupling of electron-rich aromatic rings appears to be unsuccessful only in instances where the benzylic position is capable of forming a cation, is deactivated (i.e., carbonyl), or is capable of oxidation.[11,13,20] Thus, oxidation of dithiane **6a** with either VOF_3 or $Mn(acac)_3$ or by anodic oxidation efficiently provided dihydronaphthalene **9**, without any indication of biaryl coupling. Although the biaryl couplings require a strong acid medium [e.g., trifluoroacetic acid (TFA)], the dithiane underwent cyclization even in the absence of TFA. Dihydronaphthalene **9** could be further oxidized to the naphthalene by either overexposure

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