Journal of Chemical Ecology, Vol. 27, No. 2, 2001

SYNTHESIS AND ANTIALGAL ACTIVITY OF DIHYDROPHENANTHRENES AND PHENANTHRENES II: MIMICS OF NATURALLY OCCURRING COMPOUNDS IN *Juncus effusus*

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(Received November 15, 1999; accepted September 30, 2000)

Abstract—9,10-Dihydrophenanthrenes and phenanthrenes, mimics of natural compounds with strong antialgal activity, have been synthesized through cross-coupling by zerovalent Ni of 1-(2-iodo-5-methoxy)-phenylethanol or 2-iodo-5-methoxyacetophenone with iodoxylenes. The synthetic compounds had a hydroxyl or a methoxyl group at C-2 and two methyls in the C ring. Assays on the green alga *Selenastrum capricornutum* showed that all the compounds, except 2-methoxy-5,7-dimethylphenanthrene, caused strong inhibition of algal growth at 10^{-4} M. 2-Hydroxy-7,8-dimethyl-9,10-dihydrophenanthrene and 2-methoxy-5,6-dimethylphenanthrene fully inhibited growth at 10^{-5} M.

Key Words—*Juncus effusus*, phenanthrenes, 9,10-dihydrophenanthrenes, cross-coupling algicides, *Selenastrum capricornutum*.

INTRODUCTION

We reported in a previous paper (DellaGreca et al., 2000) the synthesis of 9,10-dihydrophenanthrenes 1a–1l and phenanthrenes 2a–2l, mimics of natural com-

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0098-0331/01/0200-0257$19.50/0

pounds isolated from the wetland plant, *Jancus effusus* (DellaGreca et al., 1992, 1993, 1995a,b, 1997). The compounds have the common feature of a hydroxyl or a methoxyl group at the C-2 position of the A ring, while a methyl group is located at different positions of the C ring. Synthesis was based on cross-coupling of 1-(2-iodo-5-methoxy)-phenylethanol (**3**) with the three isomeric iodotoluenes. The compounds, except 7-methyl-2-methoxyphenanthrene (**2g**), showed strong antialgal activity in assays of the freshwater green alga *Selenastrum capricornutum* at 10^{-4} M concentration. Most of them also retained strong activity at 10^{-5} M.

In pursuing the study of the structure–activity relationship, we have now synthesized all the isomeric phenanthrenes and 9,10-dihydrophenanthrenes with a hydroxyl or a methoxyl at C-2 bearing two methyls in the C ring. The synthesis was based on the cross-coupling of iodoarenes by zerovalent nickel (Semmelhack et al., 1981).

METHODS AND MATERIALS

Chemicals. 3-Iodo-4-methylbenzoic acid and iodobenzenes were obtained commercially (Aldrich). 1-(2-Iodo-5-methoxy)-phenylethanol (**3**) was prepared as reported by DellaGreca et al. (2000).

General Experimental Procedures. NMR spectra were recorded at 400 MHz for ^{1}H and 100 MHz for ^{13}C on a Bruker AC 400 spectrometer in $CDCl_3$ solutions. One-bond and long-range H-C COSY experiments were performed with the XHCORR microprogram with delays corresponding to $J_{C,H}$ = 160 Hz and 8 Hz, respectively. HPLC was performed on a Varian Vista 5500 with a UV detector.

*Synthesis of 2-Hydroxy-6,7-dimethyl-9,10-dihydrophenanthrene (**1t**), 2-Hydroxy-7,8-dimethyl-9,10-dihydrophenanthrene (**1x**), 2-Hydroxy-6,7-dimethylphenanthrene (**2t**), and 2-Hydroxy-7,8-dimethylphenanthrene (**2x**).* To a 50-ml three-necked flask, zinc dust (392 mg, 6 mmol washed with 2 N HCl, H_2O, EtOH, Me_2CO, Et_2O, and dried in an oven at 120°C), $NiCl_2$ (784 mg, 6 mmol), PPh_3 (6.3 g, 24 mmol), and dry DMF (10 ml) were added. The mixture was warmed at 40°C under N_2 and stirred for 1 hr. A solution of **3** (834 mg, 3 mmol) and iodo-3,4-dimethylbenzene (696 mg, 3 mmol) in dry DMF (5 ml) was added at once, and the reaction mixture was kept at 40°C for 6 hr. Then 2 N NH_4OH was added and the mixture was extracted with Et_2O. After evaporation the residue was chromatographed on silica gel (benzene–Et_2O 19 : 1) to afford biphenyl **5b** (360 mg, 1.4 mmol, 47%): ^{1}H NMR δ 7.21 (1H, d, J = 2.3 Hz, H-3), 6.84 (1H, dd, J = 2.3 and 8.4 Hz, H-5), 7.15 (1H, d, J = 8.4 Hz, H-6), 7.05 (1H, d, J = 2.3 Hz, H-2′), 7.16 (1H, d, J = 8.5 Hz, H-5′), 7.01 (1H, dd, J = 2.3 and 8.5 Hz, H-6′), 5.00 (1H, q, J = 6.4 Hz, H-7), 1.39 (3H, d, J = 6.4 Hz, H-8), 3.86 (3H, s, OMe), 2.30 (3H, s, Me), 2.31 (3H, s, Me).

To a solution of **5b** (360 mg, 1.4 mmol) in dry xylene (1 ml), I_2 (20 mg, 0.08 mol) was added and the mixture was kept at 140°C for 6 hr. Addition of 10% aq $NaHSO_3$ and extraction with Et_2O gave a residue that was chromatographed on silica gel (hexane) to give **6b** (265 mg, 1.1 mmol, 80%): ^{1}H NMR δ 7.24 (1H, d, J = 2.2 Hz, H-3), 6.94 (1H, dd, J = 2.2 and 8.4 Hz, H-5), 7.19 (1H, d, J = 8.4 Hz, H-6), 7.21 (1H, d, J = 2.4 Hz, H-2′), 7.28 (1H, d, J = 8.4 Hz, H-5′), 7.16 (1H, dd, J = 2.4 and 8.5 Hz, H-6′), 6.76 (1H, dd, J = 10.5 and 17.6 Hz, H-7), 5.24 (1H, dd, J = 1.8 and 10.5 Hz, H-8), 5.75 (1H, dd, J = 1.8 and 17.6 Hz, H-8), 3.91 (3H, s, OMe), 2.37 (6H, s, Me).

A sample of **6b** (130 mg, 0.55 mmol) in dry benzene (6.5 ml) in a Pyrex flask was irradiated under an air atmosphere with a 450-W Hanovia lamp at room temperature for 30 min with magnetic stirring to give a mixture of **2s** and **2w** (63 mg, 0.30 mmol, 54%) along with unreacted **6b** (52 mg). **2s** and **2w** were separated by HPLC-NH_2 (hexane–isopropyl ether 98.5 : 1.5) **2s** (28 mg) had: ^{1}H NMR δ 7.22–7.36 (2H, m, H-1 and H-3), 8.60 (1H, d, J = 9.1 Hz, H-4), 8.36 (1H, s, H-5), 7.63 (1H, s, H-8), 7.63 (1H, d, J = 7.4 Hz, H-9), 7.48 (1H, d, J = 7.4 Hz, H-10), 3.97 (3H, s, OMe), 2.55 (3H, s, Me), 2.49 (3H, s, Me); ^{13}C NMR δ 117.0 (C-1), 157.2 (C-2), 108.9 (C-3), 124.6 (C-4), 122.8 (C-5), 134.9 (C-6), 133.8 (C-7), 129.5 (C-8), 125.8 (C-9), 127.3 (C-10), 132.6 (C-1a), 125.9 (C-4a), 127.9 (C-5a), 133.9 (C-8a) 55.6 (OMe), 20.8 (Me), 22.9 (Me). Compound **2w** (27 mg) had: ^{1}H NMR δ 7.22–7.36 (2H, m, H-1 and H-3), 8.62 (1H, d, J = 9.3 Hz, H-4), 8.39 (1H, d, J = 9.3 Hz, H-5), 7.71 (1H, d, J = 9.3 Hz, H-6), 8.02 (1H, d, J = 8.4 Hz, H-9), 7.57 (1H, d, J = 8.4 Hz, H-10), 3.98 (3H, s, OMe), 2.55 (3H, s, Me), 2.83 (3H, s, Me); ^{13}C NMR δ 117.3 (C-1), 157.3 (C-2), 108.5 (C-3), 124.3 (C-4), 120.0 (C-5), 128.9 (C-6), 133.9 (C-7), 136.1 (C-8), 123.8 (C-9), 126.4 (C-10), 132.7 (C-1a), 126.6 (C-4a), 128.1 (C-5a), 129.8 (C-8a), 55.6 (OMe), 20.1 (Me), 21.0 (Me).

To a solution of **2s** (26 mg, 0.12 mmol) in dry CH_2Cl_2 (1.5 ml) cooled at −70°C, BBr_3 (100 μl) was added. Addition of 1 N $NaHCO_3$ after 3 hr and extraction with $CHCl_3$ gave a residue that was purified by preparative TLC (hexane–Et_2O 1 : 1) to give **2t** (18 mg, 0.08 mmol, 70%): ^{1}H NMR δ 7.21 (1H, d, J = 2.1 Hz, H-1), 7.19 (1H, dd, J = 2, 1 and 9.2 Hz, H-3), 8.56 (1H, d, J = 9.2 Hz, H-4), 8.34 (1H, s, H-5), 7.60 (1H, s, H-8), 7.62 (1H, d, J = 7.4 Hz, H-9), 7.46 (1H, d, J = 7.4 Hz, H-10), 2.52 (3H, s, Me), 2.45 (3H, s, Me); ^{13}C NMR δ 116.6 (C-1), 153.8 (C-2), 111.7 (C-3), 124.9 (C-4), 122.7 (C-5), 135.0 (C-6), 133.8 (C-7), 129.5 (C-8), 125.4 (C-9), 127.5 (C-10), 132.7 (C-1a), 125.8 (C-4a), 128.0 (C-5a), 133.5 (C-8a) 20.8 (Me), 21.1 (Me).

To a solution of **2w** (25 mg, 0.12 mmol) in dry CH_2Cl_2 (1.5 ml) cooled at −70°C, BBr_3 (100 μl) was added. Addition of 1 N $NaHCO_3$ after 3 hr and extraction with $CHCl_3$ gave a residue that was purified by preparative TLC (hexane–Et_2O 1 : 1) to give **2x** (17 mg, 0.09 mmol, 70%): ^{1}H NMR δ 7.21 (1H, d, J = 2.3 Hz, H-1), 7.19 (1H, dd J = 2.3 and 9.2 Hz), 8.58 (1H, d, J = 9.2 Hz,

H-4), 8.37 (1H, d, J = 9.3 Hz, H-5), 7.70 (1H, d, J = 9.3 Hz, H-6), 8.00 (1H, d, J = 8.4 Hz, H-9), 7.52 (1H, d, J = 8.4 Hz, H-10), 2.52 (3H, s, Me), 2.65 (3H, s, Me); ^{13}C NMR δ 116.9 (C-1), 154.0 (C-2), 112.0 (C-3), 124.6 (C-4), 119.9 (C-5), 128.9 (C-6), 133.9 (C-7), 136.2 (C-8), 124.0 (C-9), 126.1 (C-10), 133.1 (C-1a), 126.4 (C-4a), 128.1 (C-5a), 129.8 (C-8a), 20.1 (Me), 20.8 (Me).

To an EtOH solution (4.8 ml) of **2s** (26 mg, 0.12 mmol), $NaBH_4$ (0.3 mmol) and Et_3N (1.2 mmol) were added. The reaction mixture was irradiated for 2.5 hr with a Hanovia 450-W lamp and then HCl 10% was added. $CHCl_3$ extraction gave a crude product, which was chromatographed by preparative TLC (hexane–benzene 9 : 1) to give **1s** (13 mg, 0.06 mmol, 50%): ^{1}H NMR δ 6.72 (1H, d, J = 2.3 Hz, H-1), 6.88 (1H, dd, J = 2.3 and 8.4 Hz, H-3), 7.72 (1H, d, J = 8.2 Hz, H-4), 7.03 (1H, s, H-5), 7.49 (1H, s, H-8), 2.83 (4H, brs, H-9 and H-10), 3.85 (3H, s, OMe) 2.33 (3H, s, Me), 2.28 (3H, s, Me); ^{13}C NMR δ 112.2 (C-1), 159.1 (C-2), 113.5 (C-3), 124.5 (C-4), 124.3 (C-5), 134.9 (C-6), 134.9 (C-7), 129.4 (C-8), 28.6 (C-9), 29.8 (C-10), 137.9 (C-1a), 127.9 (C-4a), 138.9 (C-5a), 132.0 (C-8a), 55.3 (OMe), 19.7 (Me), 19.4 (Me).

BBr_3 (50 μl) treatment of **1s** (10 mg, 0.05 mmol) in dry CH_2Cl_2 (1 ml) at -70°C for 3 hr gave **1t** (7 mg, 0.03 mmol): ^{1}H NMR δ 6.74 (1H, d, J = 2.2 Hz, H-1), 6.78 (1H, dd, J = 2.2 and 8.4 Hz, H-3), 7.63 (2H, d, J = 8.4 Hz, H-4), 7.03 (1H, s, H-5), 7.47 (1H, s, H-8), 2.81 (4H, brs, H-9 and H-10), 2.32 (3H, s, Me), 2.28 (3H, s, Me); ^{13}C NMR δ 113.7 (C-1), 154.1 (C-2), 114.9 (C-3), 124.8 (C-4), 124.3 (C-5), 135.0 (C-6), 135.0 (C-7), 129.4 (C-8), 28.5 (C-9), 29.5 (C-10), 137.8 (C-1a), 127.7 (C-4a), 139.2 (C-5a), 132.0 (C-8a), 19.7 (Me), 19.4 (Me).

Photoreduction of **2w** (25 mg, 0.12 mmol), as described for **2s**, gave **1w** (11 mg, 0.06 mmol, 50%): ^{1}H NMR δ 6.79 (1H, d, J = 2.4 Hz, H-1), 6.84 (1H, dd, J = 2.4 and 8.5 Hz, H-3), 7.66 (1H, d, J = 8.5 Hz, H-4), 7.49 (1H, d, J = 8.1 Hz, H-5), 7.09 (1H, d, J = 8.1 Hz, H-6), 2.85 (4H, brs, H-9 and H-10), 3.84 (3H, s, OMe) 2.34 (3H, s, Me), 2.26 (3H, s, Me); ^{13}C NMR δ 112.3 (C-1), 158.6 (C-2), 113.0 (C-3), 125.0 (C-4), 120.6 (C-5), 128.1 (C-6), 134.9 (C-7), 134.8 (C-8), 25.3 (C-9), 29.4 (C-10), 135.1 (C-1a), 128.1 (C-4a), 138.6 (C-5a), 132.2 (C-8a), 55.3 (OMe), 15.4 (Me), 20.8 (Me).

Demethylation by BBr_3 of **1w** (10 mg, 0.06 mmol) gave **1x** (6 mg, 0.04 mmol, 67%): ^{1}H NMR δ 6.72 (1H, d, J = 2.4 Hz, H-1), 6.77 (1H, dd, J = 2.4 and 8.5 Hz, H-3), 7.61 (1H, d, J = 8.5 Hz, H-4), 7.49 (1H, d, J = 8.1 Hz, H-5), 7.11 (1H, d, J = 8.1 Hz, H-6), 2.84 (4H, brs, H-9 and H-10), 2.36 (3H, s, Me), 2.28 (3H, s, Me); ^{13}C NMR δ 113.7 (C-1), 154.6 (C-2), 114.4 (C-3), 125.3 (C-4), 120.6 (C-5), 128.1 (C-6), 134.9 (C-7), 135.2 (C-8), 25.2 (C-9), 29.5 (C-10), 135.2 (C-1a), 128.4 (C-4a), 138.7 (C-5a), 132.3 (C-8a), 15.4 (Me), 20.8 (Me).

*Synthesis of 2-Hydroxy-6,8-dimethyl-9,10-dihydrophenanthrene (**1v**) and 2-Hydroxy-6,8-dimethylphenanthrene (**2v**).* A solution of **3** (3 mmol) and iodo-3,5-dimethylbenzene (3 mmol) in dry DMF (5 ml) was added to the mixture of the active nickel complex prepared as reported above. Work-up after 9 hr at 35°C

and chromatography on silica gel (benzene–Et_2O 19 : 1) gave biaryl **5a** (273 mg, 1.1 mmol, 37%): ^{1}H NMR δ 7.24 (1H, d, J = 2.2 Hz, H-3), 6.86 (1H, dd, J = 2.2 and 8.3 Hz, H-5), 7.08 (1H, d, J = 8.3 Hz, H-6), 6.92 (3H, d, J = 2.1 Hz, H-2′ and H-4′) 7.01 (1H, brs, H-6′), 5.01 (1H, q, J = 6.2 Hz, H-7), 1.41 (3H, d, J = 6.2 Hz, H-8), 3.86 (3H, s, OMe), 2.38 (6H, s, Me).

To a solution of **5a** (270 mg, 1.1 mmol) in dry xylene (1 ml), I_2 (20 mg, 0.08 mol) was added and the mixture was kept at 140°C for 6 hr. Work-up as for **6b** gave **6a** (212 mg, 0.88 mmol, 80%): ^{1}H NMR δ 7.30 (1H, d, J = 2.2 Hz, H-3), 6.98 (1H, dd, J = 2.2 and 8.4 Hz, H-5), 7.32 (1H, d, J = 8.4 Hz, H-6), 7.09 (2H, brs, H-2′ and H-6′), 7.18 (1H, brs, H-4′), 6.88 (1H, dd, J = 10.6 and 17.5 Hz, H-7), 5.32 (1H, dd, J = 1.8 and 10.6 Hz, H-8), 5.83 (1H, dd, J-1.8 and 17.5 Hz, H-8), 3.98 (3H, s, OMe), 2.49 (6H, s, Me).

Photocyclization of **6a** (100 mg, 0.4 mmol) in an Ar atmosphere for 1 hr gave 2-methoxy-6,8-dimethyl-9,10-dihydrophenanthrene (**1u**) (74 mg, 0.3 mmol, 75%): ^{1}H NMR δ 6.81 (1H, d, J = 2.4 Hz, H-1), 6.88 (1H, dd, J = 2.4 and 8.5 Hz, H-3), 7.71 (1H, d, J = 8.5 Hz, H-4), 6.95 (1H, d, J = 2.3 Hz, H-5), 7.41 (1H, d, J = 2.3 Hz, H-7), 2.82 (4H, brs, H-9 and H-10), 3.86 (3H, s, OMe) 2.37 (3H, s, Me), 2.33 (3H, s, Me); ^{13}C NMR δ 112.3 (C-1), 158.9 (C-2), 113.2 (C-3), 125.3 (C-4), 121.8 (C-5), 135.2 (C-6), 129.4 (C-7), 134.4 (C-8), 24.5 (C-9), 29.4 (C-10), 135.6 (C-1a), 128.0 (C-4a), 138.9 (C-5a), 132.0 (C-8a), 55.3 (OMe), 21.3 (Me), 19.7 (Me). BBr_3 demethylation of **1u** (30 mg, 0.18 mmol) gave **1v** (20 mg, 0.12 mmol, 68%): ^{1}H NMR δ 6.72 (1H, d, J = 2.5 Hz, H-1), 6.78 (1H, dd, J = 2.5 and 8.3 Hz, H-3), 7.64 (1H, d, J = 8.3 Hz, H-4), 6.93 (1H, d, J = 2.3 Hz, H-5), 7.41 (1H, d, J = 2.3 Hz, H-7), 2.80 (4H, brs, H-9 and H-10), 2.39 (3H, s, Me), 2.33 (3H, s, Me); ^{13}C NMR δ 113.7 (C-1), 154.7 (C-2), 114.6 (C-3), 125.4 (C-4), 121.6 (C-5), 135.1 (C-6), 129.4 (C-7), 134.8 (C-8), 24.3 (C-9), 29.1 (C-10), 135.5 (C-1a), 128.1 (C-4a), 139.2 (C-5a), 131.9 (C-8a), 21.2 (Me), 19.7 (Me).

Photocyclization of **6a** (100 mg, 0.4 mmol) in the presence of atmospheric oxygen gave **2u** (70 mg, 0.3 mmol, 75%): ^{1}H NMR δ 7.22–7.36 (2H, m, H-1 and H-3), 8.52 (1H, d, J = 9.2 Hz, H-4), 8.30 (1H, d, J = 1.9 Hz, H-5), 7.22 (1H, d, J = 1.9 Hz, H-7), 7.91 (1H, d, J = 7.4 Hz, H-9), 7.57 (1H, d, J = 7.4 Hz, H-10), 3.98 (3H, s, OMe), 2.72 (3H, s, Me), 2.52 (3H, s, Me); ^{13}C NMR δ 117.0 (C-1), 158.2 (C-2), 108.3 (C-3), 124.6 (C-4), 120.1 (C-5), 134.7 (C-6), 123.5 (C-7), 135.9 (C-8), 125.3 (C-9), 128.7 (C-10), 133.3 (C-1a), 124.8 (C-4a), 127.8 (C-5a), 130.7 (C-8a), 55.4 (OMe), 22.0 (Me), 19.8 (Me). Demethylation of **2u** (35 mg, 0.2 mmol) by BBr_3 gave **2v** (26 mg, 0.14 mmol, 70%): ^{1}H NMR δ 7.22–7.36 (2H, m, H-1 and H-3), 8.61 (1H, d, J = 9.2 Hz, H-4), 8.28 (1H, d, J = 1.9 Hz, H-5), 7.22 (1H, d, J = 1.9 Hz, H-7), 7.91 (1H, d, J = 7.4 Hz, H-9), 7.58 (1H, d, J = 7.4 Hz, H-10), 2.71 (3H, s, Me), 2.57 (3H, s, Me); ^{13}C NMR δ 117.1 (C-1), 153.0 (C-2), 111.5 (C-3), 124.9 (C-4), 120.2 (C-5), 134.9 (C-6), 123.5 (C-7), 136.0 (C-8), 125.3 (C-9), 128.7 (C-10), 133.7 (C-1a), 124.6 (C-4a), 127.8 (C-5a), 130.4 (C-8a), 22.2 (Me), 20.0 (Me).

*Synthesis of 2-Hydroxy-5,6-dimethyl-9,10-dihydrophenanthrene (**1n**) and 2-Hydroxy-5,6-dimethylphenanthrene (**2n**).* 2-Iodo-5-methoxyacetophenone (830 mg, 3 mmol), obtained by reaction of equimolar amounts of 3-methoxyacetophenone, I_2, CF_3COOAg, and iodo-2,3-dimethylbenzene (696 mg, 3 mmol) were added to a flask containing active Ni, prepared as described for **1t**. The reaction mixture was kept under N_2 at 40°C for 50 hr with magnetic stirring. Addition of 2 N NH_4OH and extraction with Et_2O gave crude **4c**, which was purified by silica gel column chromatography (hexane–Et_2O 19 : 1). Pure **4c** (300 mg, 1.3 mmol, 43%) gave the following data: ^{1}H NMR δ 7.20 (1H, d, J = 2.3 Hz, H-3), 6.97 (1H, dd, J = 2.3 and 8.3 Hz, H-5), 7.16 (1H, d, J = 8.3 Hz, H-6), 7.02–7.18 (3H, m, H-4′–H-6′), 3.89 (3H, s, OMe), 2.33 (3H, s, H-8), 2.04 (3H, s, Me), 1.92 (3H, s, Me). A pure sample of **4c** (200 mg), dissolved in MeOH (10 ml), was treated with $NaBH_4$ excess at 40°C for 20 min. The reaction mixture was added to 10% HCl and extracted with Et_2O. Preparative TLC (benzene–Et_2O, 47 : 3) gave pure **5c** (180 mg): ^{1}H NMR δ 7.18 (1H, d, J = 2.1 Hz, H-3), 6.97 (1H, dd, J = 2.1 and 8.4 Hz, H-5), 7.14 (1H, d, J = 8.4 Hz, H-6), 7.00–7.23 (3H, m H-4′–H-6′), 4.60 and 4.72 (1H, q, J = 6.2 Hz, H-7), 1.29 (3H, d, J = 6.2 Hz, H-8, 3.89 (3H, s, OMe), 2.01 and 1.96 (3H, s, Me), 2.36 (3H, s, Me).

To a solution of **5c** (180 mg, 0.7 mmol) in dry xylene (1 ml), I_2 (20 mg, 0.08 mol) was added, and the mixture was kept at 140°C for 6 hr. Work-up as for **6b** gave **6c** (143 mg, 0.6 mmol, 67%): ^{1}H NMR δ 6.90 (1H, dd, J = 2.3 and 8.3 Hz, H-5), 6.95–7.20 (5H, m), 6.41 (1H, dd, J = 11.0 and 17.1 Hz, H-7), 5.64 (1H, dd, J = 1.8 and 17.1 Hz, H-8), 5.11 (1H, dd, J = 1.8 and 11.0 Hz, H-8), 3.90 (3H, s, OMe), 2.35 (3H, s, Me), 1.98 (3H, s, Me). Photocyclization of **6c** (73 mg, 0.3 mmol) in an Ar atmosphere for 1 hr gave 2-methoxy-5,6-dimethyl-9,10-dihydrophenanthrene (**1m**) (55 mg, 0.2 mmol, 67%): ^{1}H NMR δ 6.86 (1H, d, J = 2.1 Hz, H-1), 6.84 (1H, dd, J = 2.1 and 8.5 Hz, H-3), 7.55 (1H, d, J = 8.5 Hz, H-4), 7.03 (2H, brs, H-7 and H-8), 2.73 (4H, brs, H-9 and H-10), 3.87 (3H, s, OMe) 2.50 (3H, s, Me), 2.35 (3H, s, Me); ^{13}C NMR δ 111.2 (C-1), 159.0 (C-2), 113.4 (C-3), 130.4 (C-4), 135.1 (C-5), 136.7 (C-6), 128.1 (C-7), 125.0 (C-8), 31.0 (C-9), 31.0 (C-10), 137.8 (C-1a), 128.2 (C-4a), 141.8 (C-5a), 132.8 (C-8a), 55.6 (OMe), 21.4 (Me), 19.4 (Me). BBr_3 demethylation of **1m** (45 mg, 0.17 mmol) gave **1n** (30 mg, 0.12 mmol, 66%): ^{1}H NMR δ 6.78 (1H, d, J = 2.4 Hz, H-1), 6.75 (1H, dd, J = 2.4 and 8.3 Hz, H-3), 7.48 (1H, d, J = 8.3 Hz, H-4), 7.03 (2H, brs, H-7 and H-8), 2.71 (4H, brs, H-9 and H-10), 2.49 (3H, s, Me), 2.35 (3H, s, Me); ^{13}C NMR δ 112.3 (C-1), 154.1 (C-2), 114.4 (C-3), 130.2 (C-4), 135.0 (C-5), 136.3 (C-6), 127.7 (C-7), 124.7 (C-8), 30.4 (C-9), 30.6 (C-10), 136.8 (C-1a), 127.9 (C-4a), 142.3 (C-5a), 132.6 (C-8a), 21.0 (Me), 19.0 (Me).

Photocyclization of **6c** (70 mg, 0.3 mmol) in the presence of atmospheric oxygen gave **2m** (50 mg, 0.18 mmol, 65%): ^{1}H NMR δ 7.28 (1H, d, J = 2.3 Hz, H-1), 7.21 (1H, dd, J = 2.3 and 9.2 Hz, H-3), 8.68 (1H, d, J = 9.2 Hz, H-4), 7.64 (1H, d, J = 8.7 Hz, H-7), 7.65 (1H, d, J = 8.7 Hz, H-8), 7.57 (1H, d, J = 7.9 Hz,

H-9), 7.38 (1H, d, J = 7.9 Hz, H-10), 3.98 (3H, s, OMe), 2.94 (3H, s, Me), 2.57 (3H, s, Me); ^{13}C NMR δ 114.8 (C-1), 157.4 (C-2), 108.8 (C-3), 129.8 (C-4), 135.4 (C-5), 136.4 (C-6), 128.2 (C-7), 125.8 (C-8), 128.0 (C-9), 126.3 (C-10), 132.6 (C-1a), 125.1 (C-4a), 129.7 (C-5a), 131.1 (C-8a), 55.4 (OMe), 22.0 (Me), 21.7 (Me). Demethylation of **2m** (50 mg, 0.18 mmol) by BBr_3 gave **2n** (30 mg, 0.12 mmol, 63%): ^{1}H NMR δ 7.27 (1H, d, J = 2.3 Hz, H-1), 7.15 (1H, dd, J = 2.3 and 9.2, H-3), 8.65 (1H, d, J = 9.2 Hz, H-4), 7.52 (1H, d, J = 8.6 Hz, H-7), 7.63 (1H, d, J = 8.6 Hz, H-8), 7.63 (1H, d, J = 7.9 Hz, H-9), 7.39 (1H, d, J = 7.9 Hz, H-10), 2.92 (3H, s, Me), 2.55 (3H, s, Me); ^{13}C NMR δ 114.4 (C-1), 153.1 (C-2), 111.7 (C-3), 130.0 (C-4), 135.3 (C-5), 136.5 (C-6), 128.3 (C-7), 126.1 (C-8), 127.9 (C-9), 125.2 (C-10), 132.4 (C-1a), 125.4 (C-4a), 129.8 (C-5a), 130.9 (C-8a), 21.8 (Me), 21.6 (Me).

*Synthesis of 2-Hydroxy-5,7-dimethyl-9,10-dihydrophenanthrene (**1p**) and 2-Hydroxy-5,7-dimethylphenanthrene (**2p**).* 2-Iodo-5-methoxyacetophenone (830 mg, 3 mmol) and iodo-2,3-dimethylbenzene (690 mg, 3 mmol) were cross coupled as described for **1n**. The reaction mixture was kept under N_2 at 40°C for 45 hr under magnetic stirring. Work-up gave **4d**, which was purified by column chromatography (hexane–Et_2O 9 : 1). Pure **4d** (350 mg, 1.5 mmol, 50%) gave the following data: ^{1}H NMR δ 7.00–7.11 (4H, m, H-3–H-6, H-5′), 7.19 (1H, d, J = 2.4 Hz, H-3′), 7.16 (1H, dd, J = 2.4 and 8.3 Hz, H-6′), 3.89 (3H, s, OMe), 2.37 (3H, s, H-8), 2.11 (3H, s, Me), 1.94 (3H, s, Me). $NaBH_4$ excess reduction of **4d** (300 mg, 1.3 mmol) gave crude **5d**, purified by preparative TLC (benzene–Et_2O 4 : 1). **5d** (270 mg, 1.1 mmol, 90%) had: ^{1}H NMR δ 7.20 (1H, d, J = 2.7 Hz, H-3), 6.85 (1H, dd, J = 2.7 and 8.4 Hz, H-5), 6.96–7.12 (4H, m, H-6, H-4′–H-6′), 4.61 and 4.75 (1H, q, J = 6.5 Hz, H-7), 1.30 and 1.32 (3H, d, J = 6.5 Hz, H-8), 3.89 (3H, s, OMe), 2.06 and 2.02 (3H, s, Me), 2.38 (3H, s, Me).

To a solution of **5d** (270 mg, 1.1 mmol) in dry xylene (1 ml), I_2 (30 mg, 0.14 mmol) was added and the mixture was kept at 140°C for 5 hr. Work-up as for **6b** gave **6d**, purified by preparative TLC (hexane), (217 mg, 0.9 mmol, 81%): ^{1}H NMR δ 7.19 (1H, d, J = 2.3 Hz, H-3), 6.88 (1H, dd, J = 2.3 and 8.6, H-5), 7.00–7.10 (4H, m, H-6, H-3′–H-6′), 6.42 (1H, dd, J = 11.0 and 17.1 Hz, H-7), 5.65 (1H, dd, J = 1.8 and 17.1 Hz, H-8), 5.10 (1H, dd, J = 1.8 and 11.0 Hz, H-8), 3.89 (3H, s, OMe), 2.38 (3H, s, Me), 2.03 (3H, s, Me).

Photocyclization of **6d** (100 mg, 0.4 mmol) in an Ar atmosphere for 1 hr gave 2-methoxy-5,6-dimethyl-9,10-dihydrophenanthrene (**1o**) (75 mg, 0.3 mmol, 75%): ^{1}H NMR δ 6.87 (1H, d, J = 2.1 Hz, H-1), 6.83 (1H, dd, J = 2.1 and 8.5 Hz, H-3), 7.61 (1H, d, J = 8.5 Hz, H-4), 7.02 (1H, brs, H-6), 6.95 (1H, brs, H-8), 2.74 (4H, brs, H-9 and H-10), 3.87 (3H, s, OMe) 2.59 (3H, s, Me), 2.34 (3H, s, Me); ^{13}C NMR δ 110.8 (C-1), 158.2 (C-2), 113.2 (C-3), 131.2 (C-4), 134.0 (C-5), 129.0 (C-6), 136.0 (C-7), 126.3 (C-8), 30.5 (C-9), 30.7 (C-10), 138.8 (C-1a), 127.9 (C-4a), 141.3 (C-5a), 131.4 (C-8a), 55.2 (OMe), 22.9 (Me), 20.9 (Me). BBr_3 demethylation of **1o** (45 mg, 0.17 mmol) gave **1p** (30 mg, 0.12 mmol,

66%): ^{1}H NMR δ 6.77 (1H, d, J = 2.4 Hz, H-1), 6.74 (1H, dd, J = 2.4 and 8.3 Hz, H-3), 7.52 (1H, d, J = 8.3 Hz, H-4), 6.99 (1H, brs, H-6), 6.93 (1H, brs, H-8), 2.71 (4H, brs, H-9 and H-10), 2.57 (3H, s, Me), 2.33 (3H, s, Me); ^{13}C NMR δ 1124 (C-1), 153.8 (C-2), 114.4 (C-3), 131.1 (C-4), 133.7 (C-5), 129.2 (C-6), 135.6 (C-7), 126.3 (C-8), 30.3 (C-9), 30.6 (C-10), 139.0 (C-1a), 127.9 (C-4a), 141.8 (C-5a), 131.1 (C-8a), 22.9 (Me), 20.9 (Me).

Photocyclization of **6c** (100 mg, 0.4 mmol) in the presence of atmospheric oxygen gave **2o** (73 mg, 0.3 mmol, 75%): ^{1}H NMR δ 7.22–7.38 (3H, m, H-1, H-3 and H-10), 8.89 (1H, d, J = 9.0 Hz, H-4), 7.67 (2H, s, H-6 and H-8), 7.64 (1H, d, J = 8.4 Hz, H-9), 4.00 (3H, s, OMe), 3.13 (3H, s, Me), 2.55 (3H, s, Me); ^{13}C NMR δ 115.5 (C-1), 157.1 (C-2), 109.3 (C-3), 134.6 (C-4), 134.9 (C-5), 128.5 (C-6), 134.6 (C-7), 127.3 (C-8), 128.2 (C-9), 126.8 (C-10), 133.0 (C-1a), 126.2 (C-4a), 128.1 (C-5a), 131.4 (C-8a), 55.4 (OMe), 27.3 (Me), 21.1 (Me). Demethylation of **2o** (36 mg, 0.2 mmol) by BBr_3 gave **2p** (27 mg, 0.14 mmol, 70%): ^{1}H NMR δ 7.26 (1H, d, J = 1.9 Hz, H-1), 7.21 (1H, dd, J = 1.9 and 9.2, H-3), 8.81 (1H, d, J = 9.2 Hz, H-4), 7.68 (2H, s, H-6 and H-8), 7.58 (1H, d, J = 8.4 Hz, H-9), 7.30 (1H, d, J = 8.4 Hz, H-10), 3.01 (3H, s, Me), 2.51 (3H, s, Me); ^{13}C NMR δ 115.2 (C-1), 152.9 (C-2), 112.1 (C-3), 132.9 (C-4), 134.9 (C-5), 128.6 (C-6), 134.5 (C-7), 127.2 (C-8), 128.1 (C-9), 126.0 (C-10), 133.1 (C-1a), 126.2 (C-4a), 127.5 (C-5a), 130.2 (C-8a), 27.2 (Me), 20.9 (Me).

*Synthesis of 2-Hydroxy-5,8-dimethyl-9,10-dihydrophenanthrene (**1r**) and 2-Hydroxy-5,8-dimethyl-phenanthrene (**2r**).* Equimolar amounts of methyl 3-iodo-4-methylbenzoate (830 mg, 3 mmol), obtained from 3-iodo-4-methylbenzoic acid by CH_2N_2 treatment in MeOH, and **3** (830 mg, 3 mmol) were added to the flask containing the active Ni complex. After 35 hr at 40°C in N_2 atmosphere, the reaction mixture was worked up as previously described and chromatography on a silica gel column (hexane–Et_2O, 7 : 3) gave diastereoisomeric biphenyls **5e** (245 mg, 1 mmol 34%): ^{1}H NMR δ 7.31 (1H, d, J = 2.3 Hz, H-3), 6.91 (1H, dd, J = 2.3 and 8.4 Hz, H-5), 7.08 (1H, d, J = 8.4 Hz, H-6), 7.31 (1H, d, J = 8.4 Hz, H-3′), 7.92 (1H, dd, J = 2.1 and 8.4 Hz, H-4′), 7.85 (1H, d, J = 2.1 Hz, H-6′), 4.51 and 4.69 (1H, q, J = 6.5 Hz, H-7), 1.26 and 1.28 (3H, d, J = 6.5 Hz, H-8), 3.87 (6H, s, OMe), 2.10 and 2.14 (3H, s, Me). Dehydration of **5e** (245 mg, 1 mmol) as reported gave **6e**, purified by silica gel column chromatography (hexane–Et_2O, 4 : 1) (205 mg, 0.8 mmol, 80%): ^{1}H NMR δ 7.20 (1H, d, J = 2.3 Hz, H-3), 6.89 (1H, dd, J = 2.3 and 8.4 Hz, H-5), 7.07 (1H, d, J = 8.4 Hz, H-6), 7.31 (1H, d, J = 8.4 Hz, H-3′), 7.99 (1H, dd, J = 2.1 and 8.4 Hz, H-4′), 7.81 (1H, d, J = 2.1 Hz, H-6′), 6.32 (1H, dd, J = 11.0 and 17.1 Hz, H-7), 5.68 (1H, dd, J = 1.8 and 17.1 Hz, H-8), 5.13 (1H, dd, J = 1.8 and 11.0 Hz, H-8), 3.89 (6H, s, OMe), 2.11 (3H, s, Me).

A pure sample of **6e** (200 mg, 0.8 mmol) in dry benzene (6.5 ml) in a Pyrex flask was irradiated under air atmosphere with a 450-W Hanovia lamp at room temperature for 5 hr with magnetic stirring to give **2y** (150 mg, 0.6 mmol,

75%): ^{1}H NMR δ 7.20–7.34 (2H, m, H-1 and H-3), 8.67 (1H, d, J = 8.7, H-4), 7.51 (1H, d, J = 8.5 Hz, H-6), 7.99 (1H, d, J = 8.5 Hz, H-7), 8.78 (1H, d, J = 8.0 Hz, H-9), 7.77 (1H, d, J = 8.0 Hz, H-10), 4.00 (6H, s, OMe), 3.16 (3H, s, Me). A sample of **2y** (115 mg, 0.6 mmol) dissolved in dry toluene (3 ml) was treated with Red-Al solution (3 mmol) for 2 hr. NaOH (2 N) was added and the crude product was extracted with Et_2O and chromatographed on silica gel (hexane–Et_2O 9 : 1) to give **2q** (90 mg, 0.45 mmol, 75%): ^{1}H NMR δ 7.22–7.38 (3H, m, H-1, H-3 and H-7), 8.87 (1H, d, J = 9.0 Hz, H-4), 7.40 (1H, d, J = 8.8 Hz, H-6), 8.00 (1H, d, J = 7.6 Hz, H-9), 7.58 (1H, d, J = 7.6 Hz, H-10), 4.00 (3H, s, OMe), 3.11 (3H, s, Me), 2.75 (3H, s, Me); ^{13}C NMR δ 115.3 (C-1), 157.2 (C-2), 108.7 (C-3), 130.7 (C-4), 134.8 (C-5), 129.2 (C-6), 127.2 (C-7), 134.3 (C-8), 124.0 (C-9), 126.4 (C-10), 132.7 (C-1a), 125.8 (C-4a), 128.5 (C-5a), 132.9 (C-8a), 55.3 (OMe), 274 (Me), 20.3 (Me). Demethylation of **2q** (40 mg, 0.2 mmol) by BBr_3 gave **2r** (35 mg, 0.18 mmol, 90%): ^{1}H NMR δ 7.28 (1H, d, J = 1.9 Hz, H-1), 7.18 (1H, dd, J = 1.9 and 9.2, H-3), 8.81 (1H, d, J = 9.2 Hz, H-4), 7.65 (1H, d, J = 8.5 Hz, H-6), 7.30 (1H, d, J = 8.5 Hz, H-7), 7.95 (1H, d, J = 7.7 Hz, H-9), 7.35 (1H, d, J = 7.7 Hz, H-10), 3.09 (3H, s, Me), 2.73 (3H, s, Me); ^{13}C NMR δ 115.1 (C-1), 153.1 (C-2), 111.7 (C-3), 130.8 (C-4), 134.8 (C-5), 129.6 (C-6), 126.5 (C-7), 134.8 (C-8), 124.3 (C-9), 126.0 (C-10), 132.5 (C-1a), 126.2 (C-4a), 128.1 (C-5a), 132.9 (C-8a), 27.4 (Me), 20.3 (Me).

A sample of **2q** (40 mg, 0.2 mmol) was photoreduced as reported for **2s** to give **1q** (30 mg, 0.15 mmol, 75%): ^{1}H NMR δ 6.85 (1H, d, J = 2.1 Hz, H-1), 6.83 (1H, dd, J = 2.1 and 8.5 Hz, H-3), 7.58 (1H, d, J = 8.5 Hz, H-4), 7.11 (1H, d, J = 8.1 Hz, H-6), 7.01 (1H, d, J = 8.1 Hz, H-7), 2.72 (4H, brs, H-9 and H-10), 3.87 (3H, s, OMe) 2.58 (3H, s, Me), 2.33 (3H, s, Me); ^{13}C NMR δ 110.7 (C-1), 158.1 (C-2), 112.7 (C-3), 129.5 (C-4), 134.3 (C-5), 129.5 (C-6), 127.9 (C-7), 131.3 (C-8), 26.0 (C-9), 30.0 (C-10), 137.4 (C-1a), 127.9 (C-4a), 141.4 (C-5a), 132.1 (C-8a), 55.2 (OMe), 22.9 (Me), 19.9 (Me). BBr_3 demethylation of **1q** (20 mg, 0.1 mmol) gave **1r** (15 mg, 0.09 mmol, 90%): ^{1}H NMR δ 6.76 (1H, d, J = 2.4 Hz, H-1), 6.74 (1H, dd, J = 2.4 and 8.3 Hz, H-3), 7.51 (1H, d, J = 8.3 Hz, H-4), 7.10 (1H, d, J = 8.1 Hz, H-6), 7.00 (1H, d, J = 8.1 Hz, H-7), 2.71 (4H, brs, H-9 and H-10), 2.57 (3H, s, Me), 2.34 (3H, s, Me); ^{13}C NMR δ 112.3 (C-1), 153.7 (C-2), 114.2 (C-3), 129.4 (C-4), 134.1 (C-5), 129.3 (C-6), 128.2 (C-7), 131.6 (C-8), 26.2 (C-9), 30.2 (C-10), 137.6 (C-1a), 127.9 (C-4a), 141.8 (C-5a), 132.2 (C-8a), 22.8 (Me), 20.1 (Me).

Bioassay. The strain UTEX 1648 *Selenastrum capricornutum* was maintained on Bold basal medium (BBM) solidified with agar 1.5% in continuous light at 23°C. Fresh axenic cultures for the experiments were grown in 100-ml cylinders on the same culture medium. For growth tests, the compounds were dissolved in acetone. Each soluion (20 μl) was added to test tubes containing 6 ml of inoculated medium, giving final concentrations of 10^{-4}, 5×10^{-5}, and 10^{-5} M. Controls containing only acetone also were tested. The test tubes were

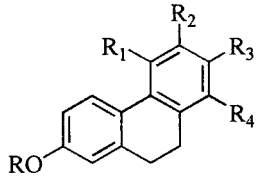
incubated at 23°C on a shaking apparatus previously described (Aliotta et al., 1991). Total irradiation of 150 μE/sec/m^2 was provided by daylight fluorescent lamps (Philips TLD 30 w/55) from below the apparatus. The photoperiod was 16 hr light and 8 hr dark. Growth of cultures was followed daily, either by measuring the absorbance increase at 550 nm with a Bausch & Lomb Spectronic 20 colorimeter or by counting the cell numbers with a Thoma blood-counting chamber. The cell numbers of the initial inocula ranged from 10^6 to 1.5×10^6/ml, corresponding to 0.05–0.06 units of absorbance. Growth experiments were carried out in triplicate. To test statistical significance of results, one-way ANOVA was performed with $P = 0.05$. For each compound, a comparison among means was performed by Student-Newman-Keuls test (SNK), with $P = 0.05$. The statistical package SPSS was used.

The index of inhibition for compounds was calculated as $[1 - (X_a/Y_a)] \times 100$ (Blankley, 1973), where X_a is the growth rate of the alga in the presence of the compound tested and Y_a is the growth rate of the control.

RESULTS AND DISCUSSION

The basic formulas and substitutions of groups for the compounds synthesized are shown in Figure 1. 1-(2-Iodo-5-methoxy)-phenylethanol (**3**), synthesized as reported in the previous paper (DellaGreca et al., 1999), was used as a starting block in the synthesis of 6,7-, 6,8-, and 7,8-dimethyl compounds. In all the reactions, equimolar amounts of **3** and iodoxylene were added at once to the reaction mixture containing the active nickel complex generated in situ by action of dust zinc on $NiCl_2(PPh_3)_2$ (Tiecco et al., 1984). Coupling of **3** with iodo-3,4-dimetilbenzene gave biphenyl **5b**, which was converted into **6b** by dehydration with I_2 in dry xylene at 140°C. All attempts to obtain 2-methoxy-6,7-dimethyl-9,10-dihydrophenanthrene (**1s**) and 2-methoxy-7,8-dimethyl-9,10-dihydrophenanthrene (**1w**) by UV irradiation of **6b** in an Ar atmosphere (Padwa et al., 1977) failed, while photocyclization of **6b** by UV irradiation in an air atmosphere easily gave a mixture of 2-methoxy-6,7-dimethylphenanthrene (**2s**) and 2-methoxy-7,8-dimethylphenanthrene (**2w**), which were separated by HPLC-NH_2. Demethylation by BBr_3 in CH_2Cl_2 for 3 hr at −70°C converted **2s** and **2w** into 2-hydroxy-6,7-dimethylphenanthrene (**2t**) and 2-hydroxy-7,8-dimethylphenanthrene (**2x**).

2-Methoxy-6,7-dimethyl-9,10-dihydrophenanthrene (**1s**) and 2-methoxy-7,8-dimethyl-9,10-dihydrophenanthrene (**1w**) were obtained from **2s** and **2w** by photoreduction with $NaBH_4$ in EtOH and Et_3N and UV irradiation (Nien-chu et al., 1984). Subsequent demethylation as above reported gave 2-hydroxy-6,7-dimethyl-9,10-dihydrophenanthrene (**1t**) and 2-hydroxy-7,8-dimethyl-9,10-dihydrophenanthrene (**1x**).



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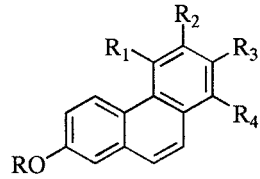

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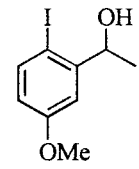
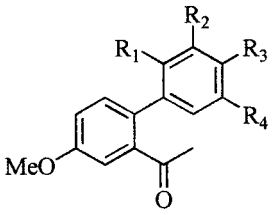


3

	R	R_1	R_2	R_3	R_4		R	R_1	R_2	R_3	R_4
a	Me	H	H	H	H	o	Me	Me	H	Me	H
b	H	H	H	H	H	p	H	Me	H	Me	H
c	Me	Me	H	H	H	q	Me	Me	H	H	Me
d	H	Me	H	H	H	r	H	Me	H	H	Me
e	Me	H	Me	H	H	s	Me	H	Me	Me	H
f	H	H	Me	H	H	t	H	H	Me	Me	H
g	Me	H	H	Me	H	u	Me	H	Me	H	Me
h	H	H	H	Me	H	v	H	H	Me	H	Me
i	Me	H	H	H	Me	w	Me	H	H	Me	Me
l	H	H	H	H	Me	x	H	H	H	Me	Me
m	Me	Me	Me	H	H	y	Me	Me	H	H	CO_2Me
n	H	Me	Me	H	H						



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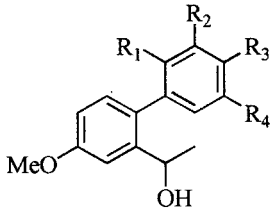

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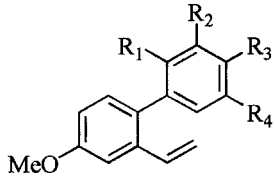

6

FIG. 1. The basic structural skeletons of compounds synthesized, and the various groups that were substituted at the positions marked by R_1, R_2, R_3, and R_4.

Coupling of **3** with iodo-3,5-dimethylbenzene gave **5a**, which, through the styrene derivative **5b** was converted by UV irradiation into 2-methoxy-6,8-dimethyl-9,10-dihydrophenanthrene (**1u**) in an argon atmosphere and into 2-methoxy-6,8-dimethylphenanthrene (**2u**) in the presence of atmospheric oxygen. Demethylation of **1u** and **2u** afforded 2-hydroxy-6,8-dimethyl-9,10-dihydrophenanthrene (**1v**) and 2-hydroxy-6,8-dimethylphenanthrene (**2v**).

The synthesis of dimethyl compounds with a methyl at C-5 by cross-coupling of **3** with the right iodoxylene failed as the steric hindrance of

the methyl caused long reaction times, and in such conditions the primary process was replacement of iodine by alcoholic hydrogen. The same problem was overcome in the synthesis of 2-hydroxy-5-methyl-9,10-dihydrophenanthrene (**1d**) and 2-hydroxy-5-methylphenanthrene (**2d**) by cross-coupling ortho iodotoluene with 2-iodo-5-methoxyacetophenone. In the same way, the synthesis of 2-hydroxy-5,6-dimethyl-9,10-dihydrophenanthrene (**1n**), 2-hydroxy-5,7-dimethyl-9,10-dihydrophenanthrene (**1p**), 2-hydroxy-5,6-dimethylphenanthrene (**2n**), and 2-hydroxy-5,7-dimethylphenanthrene (**2p**) was performed. Couplings of 2-iodo-5-methoxyacetophenone with iodo-2,3-dimethylbenzene and iodo-2,4-dimethylbenzene gave ketones **4c** and **4d**, respectively. $NaBH_4$ reduction afforded carbinols **5c** and **5d**. These compounds, obtained as diastereoisomeric mixtures because free rotation of the rings about each other is hindered for the presence of the methyl at C-2′, were dehydrated directly to **6c** and **6d**. Photocyclization of **6c** in the absence and in the presence of atmospheric oxygen gave 2-methoxy-5,6-dimethyl-9,10-dihydrophenanthrene (**1m**) and 2-methoxy-5,6-dimethylphenanthrene (**2m**), respectively, which were converted into **1n** and **2n** by BBr_3 demethylation. Irradiation in both the conditions of **6d** gave 2-methoxy-5,7-dimethyl-9,10-dihydrophenanthrene (**1o**) and 2-methoxy-5,7-dimethylphenanthrene (**2o**), which were demethylated to **1p** and **2p**. All attempts to synthesize 2-hydroxy-5,8-dimethyl-9,10-dihydrophenanthrene (**1r**) and 2-hydroxy-5,8-dimethylphenanthrene (**2r**) this way failed because of very long reaction times in which no coupling between 2-iodo-5-methoxyacetophenone and iodo-2,5-dimethylbenzene was obtained.

Semmelhack (1981) observed an efficient coupling of aryl halides bearing aldehyde, ketone, ester, and nitrile groups. On this basis, **3** was cross-coupled with methyl 3-iodo-4-methylbenzoate to give the corresponding diastereoisomeric biaryls **5e** that were dehydrated to **6e**. Photocyclization of **6e** in both the reported conditions gave 9,10-dihydrophenanthrene (**1y**) and phenanthrene (**2y**), which were converted into 2-methoxy-5,8-dimethyl-9,10-dihydrophenanthrene (**1q**) and 2-methoxy-5,8-dimethylphenanthrene (**2q**) by sodium bis(2-methoxyethoxy)aluminum hydride. Final demethylation of **1q** and **2q** gave **1r** and **2r**.

The 9,10-dihydrophenanthrenes and phenanthrenes purified by HPLC were assayed on *Selenastrum capricornutum* at concentrations of 10^{-5}–10^{-4} M. The compounds were stable in the assay conditions and the results had statistical significance (Tables 1 and 2). All dimethyl-9,10-dihydrophenanthrenes cause full inhibition of algal growth at 10^{-4} M concentration and no differences were observed between the hydroxy and the methoxy derivatives. High activity is maintained at 5×10^{-5} M, while at 10^{-5} M only 2-methoxy-5,6-dimethyl-9,10-dihydrophenanthrene (**1m**), 2-methoxy-5,7-dimethyl-9,10-dihydrophenanthrene (**1o**), 2-methoxy-6,8-dimethyl-9,10-dihydrophenanthrene (**1u**), and 2-methoxy-7,8-dimethyl-9,10-dihydrophenan-threne (**1w**) are still active. These compounds

TABLE 1. INHIBITION (%) OF GROWTH OF *S. capricornutum* BY SYNTHETIC 9,10-DIHYDROPHENANTHRENES[a]

	1m	**1n**	**1o**	**1p**	**1q**	**1r**	**1s**	**1t**	**1u**	**1v**	**1w**	**1x**
10^{-4} M	100 d	100 b	100 b	98 b	100 b	100 b	100 b	100 b	100 d	100 c	100 b	100 b
5×10^{-5} M	60 c	100 b	100 b	98 b	100 b	100 b	100 b	100 b	89 c	71 b	100 b	100 b
10^{-5} M	40 b	0 a	100 b	0 a	0 a	0 a	0 a	0 a	60 b	0 a	100 b	0 a
Control	0 a	0 a	0 a	0 a	0 a	0 a	0 a	0 a	0 a	0 a	0 a	0 a

[a] In each column values followed by different letters are statistically significant. Student-Newman-Keuls test; $P = 0.05$.

TABLE 2. INHIBITION (%) OF GROWTH OF *S. capricornutum* BY SYNTHETIC PHENANTHRENES

	2m	**2n**	**2o**	**2p**	**2q**	**2r**	**2s**	**2t**	**2u**	**2v**	**2w**	**2x**
10^{-4} M	100 b	98 b	0 a	100 c	98 b	100 b	70 c	100 c	100 b	70 c	75 c	100 c
5×10^{-5} M	100 b	98 b	0 a	100 c	98 b	100 b	70 c	95 b	100 b	50 b	75 c	95 b
10^{-5} M	0 a	98 b	0 a	50 b	0 a	0 a	22 b	95 b	0 a	50 b	20 b	95 b
Control	0 a	0 a	0 a	0 a	0 a	0 a	0 a	0 a	0 a	0 a	0 a	0 a

[a] In each column values followed by different letters are statistically significant. Student-Newman-Keuls test; $P = 0.05$.

have a methyl at C-5 or at C-8, and when the other methyl is at C-7, 100% activity is observed. Except for 2-methoxy-5,7-dimethylphenanthrene (**2o**), all the dimethylphenanthrenes have high activity at 10^{-4} and 5×10^{-5} M concentrations with no differences among hydroxy and methoxy derivatives. At the lowest concentration, only 2-hydroxy-5,6-dimethylphenanthrene (**2n**), 2-hydroxy-5,7-dimethylphenanthrene (**2p**), 2-hydroxy-6,7-dimethylphenanthrene (**2t**), 2-hydroxy-6,8-dimethylphenanthrene (**2v**), and 2-hydroxy-7,8-dimethyl-phenanthrene (**2x**) are active, and **2n**, **2t**, and **2x** still cause full inhibition.

In conclusion, all the synthetic phenanthrenes and 9,10-dihydrophenanthrenes cause inhibition of algal growth in the examined concentration range. A comparison among monomethyl and dimethyl compounds shows that at the highest concentration the monomethyl derivatives are less active than the dimethyl derivatives, while at the lowest concentration the activity goes in the opposite direction.

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