solution of K_2CO_3 and $KHCO_3$ prepared in D_2O. Deuterated tetrathiafulvalene, 63 mg (95%), yield mp 118–119 °C (lit.[9] mp 119 °C), was obtained: IR (KBr, cm^{-1}) 2245 (C–D).

Synthesis of Tetrakis(methylthio)tetrathiafulvalene (4). To an ice-cold solution made from 400 mg of 1 in 10 mL of dried tetrahydrofuran was added 1 mL of 5 M methanesulfenyl bromide in methylene chloride under nitrogen. After the mixture was allowed to stand at room temperature for 0.5 h, tetrabutylammonium fluoride (4 mmol) in 4 mL of tetrahydrofuran was added. The solution was allowed to stand for 10 h and then the mixture was poured into ice water and extracted with CH_2Cl_2.

The product was isolated by chromatography using Florisil silica gel eluted with the mixed solvent of chloroform and hexane (1:2 by volume). A pure red-brown liquid product (190 mg) was obtained: yield 49%; IR (film, cm^{-1}) 3060, 2960, 1480, 1420, 1310, 1260, and 800; ^1H NMR ($CDCl_3$) δ 2.46 (s); mass spectrum, *m/e* 388. Anal. Calcd for $C_{10}H_{12}S_8$: C, 30.93; H, 3.09; S, 65.98. Found: C, 31.20; H, 3.12; S, 66.25.

Synthesis of Tetrakis(methylseleno)tetrathiafulvalene (5). To an ice-cold solution of 500 mg of 1 in 10 mL of dried tetrahydrofuran was added 5 mL of 1 M methaneselenenyl bromide in CH_2Cl_2 under nitrogen. After standing in an ice bath for 20 min, tetrabutylammonium fluoride (5 mmol) in 7 mL of dried tetrahydrofuran was added. The solution was allowed to stand at room temperature for 2 h. The product was purified by chromatography using Florisil silica gel eluted with the mixed solvent of hexane and methylene chlorine (2:1 by volume). A red-brown liquid (200 mg) was obtained: yield 35%; IR (film, cm^{-1}) 3060, 2920, 1400, 1265, 1245, 860, and 760; ^1H NMR ($CDCl_3$) δ 2.40 (s); mass spectrum, *m/e* 580 (based on ^{80}Se). Anal. Calcd for $C_{10}H_{12}S_4Se_4$: C, 20.69; H, 2.07; S, 22.07; Se, 55.17. Found: C, 21.20; H, 2.15; S, 22.28; Se, 54.20.

Synthesis of Tetrakis(phenylselenyl)tetrathiafulvalene (6). This compound was prepared from 1 with benzeneselenenyl bromide by a similar method to that described in above. 6 was obtained in 58–60% yield: IR (film, cm^{-1}) 3050, 1570, 1470, 1440, 1020, 740, and 680; ^1H NMR ($CDCl_3$) δ 6.7, 6.9; mass spectrum, *m/e* 825 (based on ^{80}Se). Anal. Calcd for $C_{30}H_{20}S_4Se_4$: C, 43.66; H, 2.44; S, 15.55; Se 38.30. Found: C, 43.50; H, 2.30; S, 16.10; Se, 37.50.

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Registry No. 1, 96913-54-1; 1 (TCNQ complex), 96913-59-6; 2, 96913-55-2; 3, 96913-56-3; 4, 51501-77-0; 5, 96913-57-4; 6, 96913-58-5; TTF, 31366-25-3; TTF (deuterated), 51751-16-7; $Me_3SiC{\equiv}CSiMe_3$, 14630-40-1; $Me_3SiC{\equiv}CH$, 1066-54-2; CS_2, 75-15-0; CSe_2, 506-80-9; MeSBr, 41138-92-5; MeSeBr, 73501-41-4; PhSeBr, 34837-55-3.

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Synthesis and Physical Properties of 5,6-Dihydroxyindole

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5,6-Dihydroxyindole (2) is an important intermediate in melanogenesis, the process by which eumelanin, a black, intractable biopigment, is formed from L-3,4-dihydroxyphenylalanine (1) (Scheme I).[1] Generally, 2 is obtained either by saponification of 5,6-diacetoxyindole[2] or hydrogenolysis of 5,6-dibenzyloxyindole.[3] These methods yield only small quantities of pure 2, and until recently,[4,5] no attempts have been made to design a more efficient laboratory scale synthesis.

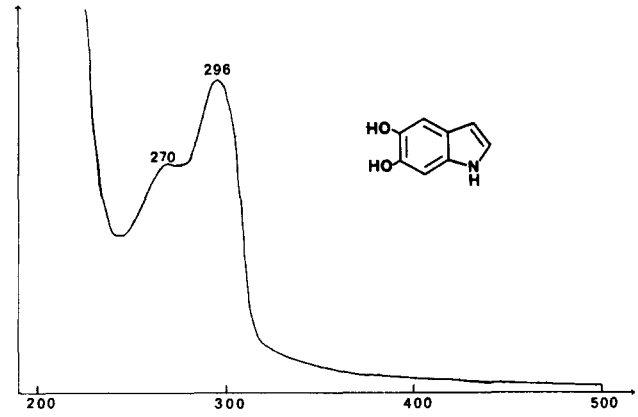
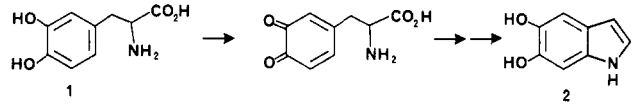
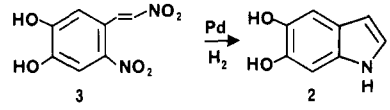


Figure 1. UV–vis spectrum of 5,6-dihydroxyindole in deaerated water.

Scheme I



Scheme II



A comprehensive summary of analytical data also is lacking, which makes in situ identification of 2 during melanogenesis difficult.

We have improved on the most recent technology: reductive cyclization of (*E*)-4,5-dihydroxy-2,β-dinitrostyrene (3) with noble metal catalysts in polar, hydroxylic solvents (Scheme II).[4,5] Herein we report these improvements and the first full summary of the physical properties of 5,6-dihydroxyindole from one source.

Results and Discussion

Catalytic hydrogenation of 3 in aqueous media gives variable yields of pure 5,6-dihydroxyindole, due to difficulty in isolation.[4] Our improvements have led to consistently higher yields of pure 2. In a typical synthesis, 3 was hydrogenated in methanol over 10% Pd/C at 50 psi, and the solvent was removed in vacuo, to give a black solid. Sonication of this material in dichloromethane produced a suspension, which yielded a golden colored solution after filtration. Concentration and chromatography (silica gel) with 1:1 dichloroethane/anhydrous diethyl ether gave nearly colorless crystals of 2.

The UV–visible spectrum (Figure 1) has λ_{max} = 296 nm in degassed H_2O (log ϵ 3.52).[6] The pK_a value for the first ionization (5-hydroxyl group) was found to be 8.9. The value for the second ionization (6-hydroxyl group) was difficult to determine accurately, due to eumelain formation at high pH, but is greater than 10.2. These assignments were based on the observation that 5,6-dihydroxy-

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(6) The value for was determined from three separately prepared samples.

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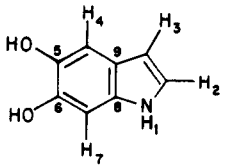
Table I. A Summary of NMR Chemical Shifts of 5,6-Dihydroxyindole



	H or C	ppm
^1H ($CDCl_3$)[a]	H_2	6.20 (d, J = 8.02 Hz)
	H_3	6.98 (d, J = 8.02 Hz)
	H_4	6.89 (s)
	H_7	6.82 (s)
^{13}C ($CDCl_3$)[a]	C_2	122.77
	C_3	101.31
	C_4	104.87
	C_5	130.65
	C_6	140.55
	C_7	98.66
	C_8	142.35
	C_9	120.96

[a] Relative to external Me_4Si.

1-methylindole[7] has ionization constants of 8.4 and 10.7 in water. Additionally, *m*- and *p*-aminophenols have pK_a's of 9.9 and 8.3, respectively.[8] This suggests that the second pK_a of **2**, which is greater than 10.2, may be ascribed to the 6-hydroxyl group.

The FT-IR spectrum was consistent with those for O–H, C–O, C–N, aromatic C–H, and N–H bonds of hydroxylated indoles, and the spectrum compares well with that for 5-hydroxyindole.[9,10]

The EI quadrapole mass spectrum has a molecular ion with *m/e* 149. The fragmentation pattern showed the loss of H_2O (*m/e* 131), HCN (*m/e* 120), and H_2O/CO (*m/e* 103), was consistent with that reported for indoles.[11]

The 300-MHz ^1H NMR showed two doublets and two singlets. Irradiation of the doublet at 6.20 ppm (J = 8.2 Hz) caused the doublet at 6.98 ppm to collapse to a singlet. The downfield signal was assigned to H-2 and the latter to H-3. Additionally, the broadened singlet at 6.89 ppm sharpened upon irradiation of the 6.98 ppm doublet, which showed this to be the H-3/H-4 pair. These data are summarized in Table I.

^{13}C NMR spectra were recorded at 75.48 MHz. Proton decoupled experiments gave spectra with eight resonance signals. The single frequency off-resonance-decoupled spectrum showed that the signals at 122.77, 101.31, 104.87, and 98.66 were sp^2 carbons singly bonded to hydrogen. Carbons 5 and 6 were distinguished by additivity rules.[12] The assignments for C-8 and C-9 were made based on comparison with known substituted indoles, and T_1 inversion-recovery experiments supported these assignments[13] (Table I).

Experimental Section

Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were obtained on a General Electric QE-300 (at 300 MHz and 75.48 MHz, respectively) NMR spectrometer, and chemical shifts are recorded relative to external tetramethylsilane. Mass spectra were obtained on a Finnegan 4000 GC/MS/DS system. A Nicolet FX-5 FT-IR infrared spectrophotometer was used to obtain IR spectra of **2** as KBr pellets. HPLC analyses were performed on a Hi-bar LiChrosorb RP-18 (10 μm) column (E. Merck), with detection at 290 nm by a Waters Associates Lambda Max variable-wavelength detector. UV–visible spectra were obtained on a Perkin-Elmer 553 B UV–visible spectrophotometer.

The method of Albert and Sargent[14] was used to determine pK_a values. The pH of an anaerobic solution of the indole in a UV cuvette was raised incrementally with 1 N NaOH, and the UV–visible spectrum was recorded.

4,5-Dihydroxy-2,β-dinitrostyrene (**3**) was synthesized from 3,4-bis(benzyloxy)benzaldehyde (Aldrich) by the method of Murphy and Banks.[4]

5,6-Dihydroxyindole (2). A mixture of 100 mg (0.44 mmol) of 4,5-dihydroxy-2,β-dinitrostyrene (**3**), 25 mL of CH_3OH, and 20 mg of 10% Pd/C was hydrogenated in a Parr apparatus at 50 psi of H_2 for 1 h. The solvent was removed in vacuo, and the resulting solid sonicated in dry CH_2Cl_2. The mixture was filtered and filtrate concentrated in vacuo and chromatographed (60–200 mesh silica gel) with 1:1 diethyl ether/dichloromethane to yield 35–50 mg (53–76%) of nearly colorless crystals: mp 141–142 °C (lit.[2] 141 °C). HPLC analysis of the sample (0.5 mL/min flow rate) gave the retention times for **2** of 10.1 min with 50% aqueous methanol as the mobile phase and 8.6 min with 40% aqueous acetonitrile.

Registry No. **2**, 3131-52-0; **3**, 96806-57-4; MeOH, 67-56-1; Pd, 7440-05-3; H_2, 1333-74-0.

(7) The sample of 5,6-dihydroxy-1-methylindole was a generous gift from Dr. G. Prota, University of Naples, Naples, Italy.

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Benzylic Oxidation Using *tert*-Butyl Hydroperoxide in the Presence of Chromium Hexacarbonyl

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Oxidation of tetralin derivatives to their corresponding α-tetralones is of considerable value in organic synthesis, and many methods have been reported for accomplishing this conversion.[1,2] Such benzylic oxidations are traditionally performed with chromic acid and have been applied to the conversion of estrones to their 6-oxo derivatives, which are of potential value in the preparation of steroid–protein conjugates useful for radioimmunoassay purposes.[3] However, low yields (1–43%) are reported for this reaction, due to a number of side products being formed by cleavage of the B and C rings.[1] Alternative

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