

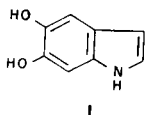
Wilson B. Lutz\*, Craig R. McNamara, Max R. Olinger, David F. Schmidt,  
Douglas E. Doster, and Mark D. Fiedler

Department of Chemistry, Manchester College,  
North Manchester, Indiana 46962  
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5,6-Carbonyldioxyindole (**4**), a melanogenic derivative of 5,6-dihydroxyindole (**1**), was synthesized by a procedure starting with 3,4-methylenedioxyindole (**2**). Compound **4** is a stable crystalline solid which is readily hydrolyzed to **1**, a key intermediate on the biosynthetic pathway from tyrosine to melanin.

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This report describes the synthesis and some of the properties of 5,6-carbonyldioxyindole (**4**), a melanogenic derivative of 5,6-dihydroxyindole (**1**). Compound **1** is an intermediate on the tyrosinase-catalyzed biosynthetic pathway from tyrosine to melanin [2]. Albinism and vitiligo are skin pigment disorders characterized by a lack of tyrosinase in the affected tissues. Once formed, **1** undergoes spontaneous oxidation and condensation to give melanin [2].



The lack of stability of **1** on storage has hampered studies of its biological activity. Some workers have therefore resorted to the use of the diacetate ester of **1** for biological studies. This approach takes advantage of the facile hydrolysis of phenolic esters to give **1** *in situ* [3,4]. Compound **4**, a cyclic carbonate ester of **1**, represents an additional compound of this type. We sought to develop a synthesis of **4** in order to evaluate the potential of this type of ester as a storable but ready source of the natural metabolite **1**.

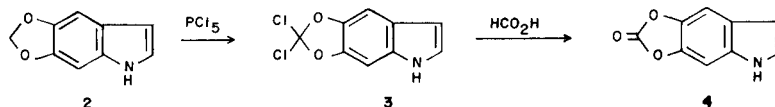
The series of reactions in Scheme I was designed to give **4** by converting 5,6-methylenedioxyindole (**2**) [5] to the dichloromethylene ether **3** with phosphorus pentachloride followed by the conversion of **3** to **4** by means of anhydrous formic acid (6 a-e). When **2** was treated sequentially with phosphorus pentachloride and formic acid, only a greenish-black tar could be obtained.

On the assumption that Scheme I failed because of the sensitivity of some indoles to strong acid [7], we developed an alternate synthesis (Scheme II) in which the indole ring is formed at a late stage and does not come into contact with strong acid. A key feature of the scheme is the ther-

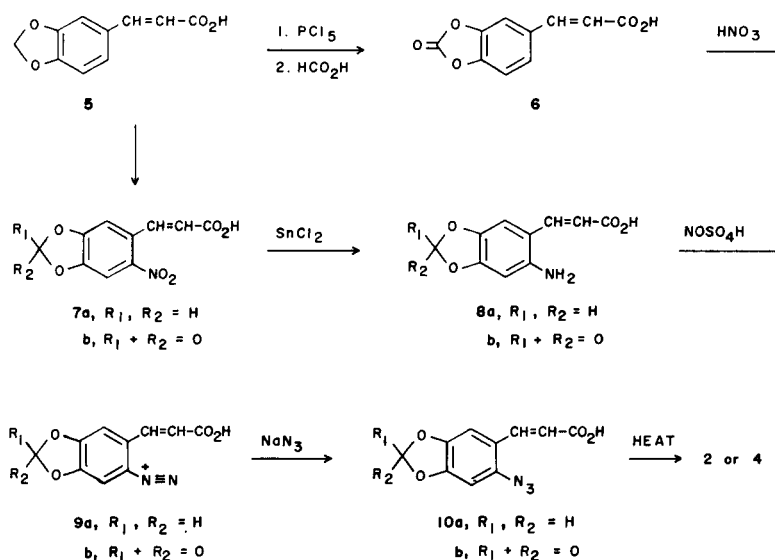
mal decomposition of an azide to effect formation of the pyrrole moiety of the indole ring system. A number of examples of this type of ring closure have been reported [8a-f]. Loss of nitrogen gives a nitrene which inserts into the C-H linkage adjacent to the carboxyl group of the cinnamic acid side chain. In order to test the feasibility of this approach, we first examined the sequence of reactions: **5** → **7a** → **8a** → **9a** → **10a** → **2**. The methylenedioxyindole **2** was obtained in good yield. Thermal decomposition of the azido acid **10a** was carried out at the boiling point of *o*-dichlorobenzene (*ca.* 179°), a temperature sufficiently high to not only generate the nitrene from the azide group but also to decarboxylate the indolecarboxylic acid presumed to be an intermediate between **10a** and **2**.

We then undertook the synthesis of cyclic carbonate **4** *via* the series of reactions: **5** → **6** → **7b** → **8b** → **9b** → **10b** → **4**. 3,4-Methylenedioxyindole (**2**) [9] was converted to the cyclic carbonate **6** of caffeic acid by sequential treatment of **5** with phosphorus pentachloride and formic acid. All remaining steps were carried out with due regard for the hydrolytic propensities of cyclic carbonate rings. Nitration of **6** with mixed acid afforded the nitro acid **7b** which was reduced to the amino acid **8b** with stannous chloride in hydrochloric acid. Compound **8b** was converted to the azido acid **10b** *via* the diazonium salt **9b**. It was necessary to carry out the diazotization of **8b** in a non-aqueous medium due to the extreme ease of hydrolysis of the cyclic carbonate ring of **9b** even in cold acidic solution. Azido acid **10b** was then heated in an appropriate solvent to effect loss of nitrogen and carbon dioxide. Slow gas evolution occurred as low as 130° but practical reaction rates required temperatures in the range 150-180°. Reasonable yields of **4** were obtained but the product was always accompanied by brownish-black byproducts. The addition of copper

SCHEME I



SCHEME II



powder seemed to suppress the formation of dark byproducts to some extent.

The direct conversion of nitro acid **7b** to **4** was also attempted. Sundberg has shown [10] that ethyl *o*-nitrocinnamate can be converted to indole-2-carboxylic acid in 19% yield by heating the nitro compound with triethyl phosphite. The phosphite ester evidently deoxygenates the nitro group to give a nitrene which then inserts into a C-H linkage of the side chain. When the same conditions were applied to **7b**, traces of **4** were detected in the reaction mixtures by means of thin-layer chromatography. Concentrations of **4** seemed to build in the reaction mixtures to a certain low level and to thereafter diminish with time. We were unable to obtain isolable amounts of **4** from such reaction mixtures despite diligent efforts to do so.

The assignment of structure **4** to the azide decomposition product is consistent with the elemental analysis, with the fact that the product can be hydrolyzed to a compound whose properties agree with published data for 5,6-dihydroxyindole, and with its spectral characteristics. The infrared spectrum shows a strong singlet in the NH region and a strong doublet in the carbonyl region. It also gives a positive reaction with the Ehrlich reagent.

Compound **4** is a crystalline solid of moderately high melting point. It is soluble in ether, dimethyl sulfoxide, ethanol, ethyl acetate, and dichloromethane. It is only sparingly soluble in cold water but is sufficiently soluble in boiling water that, by working quickly, it can be recrystallized without the occurrence of significant hydrolysis. Aqueous solutions that are even mildly alkaline hydrolyze **4** very rapidly. Such solutions become purple, then brown, and finally deposit brownish-black solids. This is in accord with similar behavior observed for diol **1** by Beer and his

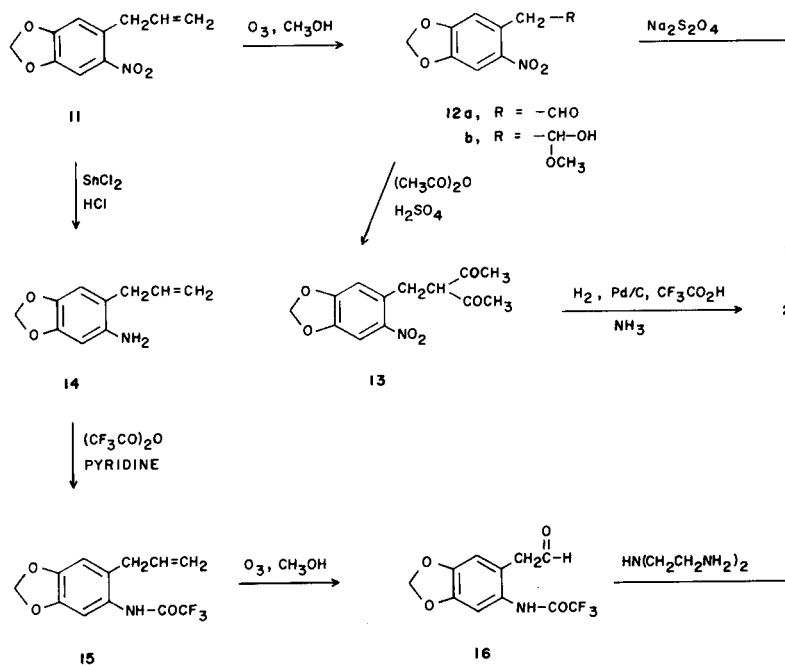
co-workers [11,12]. Compound **4** reacts with aqueous barium hydroxide to give an immediate precipitate of barium carbonate after which the solution becomes deeply colored as with other alkaline reagents.

In the crystalline state, **4** is far more stable than the parent diol. Beer *et al.* [11] found that **1** darkens appreciably within a few hours on exposure to the laboratory atmosphere and within 14 days even in a sealed container. By contrast, one sample of **4** on a sublimator cold finger underwent no visible change when exposed to humid summer air for three months. The infrared spectrum of this material was indistinguishable from the spectrum of the analytical sample and thin-layer chromatography showed that only traces of melanin-like material had formed. Substantial decomposition occurs on long term storage, however. A sample of **4** which had been stored in a plastic-capped vial for ten years on the laboratory shelf acquired a deep brown-black color. Sublimation afforded a 49% recovery of pure **4**. Storage of **4** over calcium chloride to scavenge water and volatile bases appears to extend the shelf life considerably.

The hydrolytic conversion of **4** to diol **1** evidently can occur on or within human skin. When a 4% solution of **4** in dimethyl sulfoxide was applied to the upper arm skin of one of us (W. B. L.), a zone of increased pigmentation developed within five hours and reached a maximum intensity in about twelve hours. The pigmented zone was grayish-brown and was resistant to ordinary washing. It was no longer visible after seven to ten days.

The 5,6-methylenedioxyindole (**2**) required in Scheme I was obtained in part by the iron-acetic acid reduction of  $\beta$ ,6-dinitro-3,4-methylenedioxyindole [5] and in part by

SCHEME III



the method of Scheme II. We also explored several other methods for preparing **2** in the hope that one or more of them could be modified to give **4**. These hopes were not realized but we report here the additional syntheses of **2** (see Scheme III).

In one of these methods, 6-nitrosafrole (**11**) [13] was ozonized in methanol. Reduction of the ozonolysis mixture with dimethyl sulfide [14] afforded the hemiacetal **12b** of aldehyde **12a**. The free aldehyde was readily obtained from **12b** by sublimation. Catalytic hydrogenation of **12a**

or **12b** gave **2** but in variable yield. Dithionite reduction gave similar results. Compound **2** was also obtained by means of the sequence: **11**—**12**—**13**—**2**. By this route, aldehyde **12a** (**12b** was equally suitable) was converted to the *gem*-diacetate **13** by means of acetic anhydride and a catalytic amount of concentrated sulfuric acid. Hydrogenation of **13** in trifluoroacetic acid over palladium on charcoal afforded a reduction product which, when treated with ammonia, gave **2** in 51% yield. Ammoniacal sodium dithionite also afforded **2** but in lower yield. Compound **2** was also obtained by the sequence: **11**—**14**—**15**—**16**—**2**. Compound **11** was reduced to 6-aminosafrole (**14**) [13] and the latter converted to the *N*-trifluoroacetyl derivative **15**. Ozonolysis of **15** in methanol gave the aldehyde **16** in 84-89% yield. Treatment of **16** with methanolic diethylenetriamine cleaved the trifluoroacetyl group and gave **2** in 86% yield. The indole-forming step (*i.e.* **16**—**2**) in this scheme is particularly clean, high-yielding and easy to work up.

## EXPERIMENTAL

Melting points were taken in open capillaries with a Hoover type apparatus and are uncorrected. Infrared spectra were recorded on a Beckman IR-8 spectrophotometer and run as mineral oil mulls unless otherwise noted. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN and by the Analytical and Physical Chemistry Section, Warner-Lambert Research Institute, Morris Plains, NJ. Thin-layer chromatography (tlc) was carried out on Analtech 25 × 100 mm silica gel GF plates. Nitrosylsulfuric acid was purchased from Penninsular Chemresearch, Gainesville, FL. Other reagents were purchased from Fisher Scientific Co. and Aldrich Chemical Company.

2-(3,4-Methylenedioxy-6-nitrophenyl)-1-methoxyethanol (**12b**) and 3,4-Methylenedioxy-6-nitrophenylacetaldehyde (**12a**).

A solution of 10.2 g of **11** in 110 ml of methanol was treated at 0° with a stream of ozonized air *via* a sintered diffuser until the exit gases produced a blue color with potassium iodide-starch solution (*ca.* 4 hours). Dimethyl sulfide, 10 ml, was added and the mixture kept at 25° for 30 minutes (mildly exothermic reaction). After being stored in a freezer overnight, the yellow crystals which separated were filtered and washed with cold methanol to give 7.36 g (62%) of needles, mp 96-98° dec. Recrystallization from methanol afforded pure **12a** with mp 95-96° dec; ir: 3436  $cm^{-1}$  (OH); intense purple color with 5% aqueous potassium carbonate. Some samples of **12a**, possibly a polymorphic form, melted 104-107° dec.

*Anal.* Calcd. for  $C_{10}H_{11}NO_5$ : C, 49.80; H, 4.60; N, 5.81. Found: C, 49.90; H, 4.39; N, 5.90.

Sublimation of **12b** at 95° (0.001 mm) gave **12a**, mp 96-98°; ir: (chloroform): 2717 (aldehyde CH) 1701  $cm^{-1}$  (CO); intense purple color with 5% potassium carbonate solution.

*Anal.* Calcd. for  $C_9H_9NO_5$ : C, 51.68; H, 3.37; N, 6.70. Found: C, 51.71; H, 3.44; N, 6.65.

2,4-Dinitrophenylhydrazone of **12b**.

This compound was obtained as yellow needles (acetic acid), mp 182-183.5°, tlc (toluene)  $R_f$  0.33, (ethyl acetate)  $R_f$  0.92.

Anal. Calcd. for  $C_{15}H_{11}N_3O_8$ : C, 46.28; H, 2.85; N, 17.99. Found: C, 46.34; H, 2.89; N, 17.93.

#### 1,1-Diacetoxy-2-(3,4-methylenedioxy-6-nitrophenyl)ethane (**13**).

A solution of 0.50 g of **12b** in 5 ml of acetic anhydride was treated with a small drop of concentrated sulfuric acid. The solution turned cherry red then slowly became brown. After 70 minutes at 30°, the mixture was poured onto a mixture of ice and water containing 10 g of sodium bicarbonate. The solid was filtered, washed with water, and dried *in vacuo* over calcium chloride to give 0.70 g (94%) of **13**, mp 95-99°. Two recrystallizations from 2-propanol gave pure **13**, mp 107-110°; ir: 3096 (methine CH) 1754 and 1733  $cm^{-1}$  (CO); slowly develops an intense purple color with aqueous 1 M potassium hydroxide.

Anal. Calcd. for  $C_{13}H_{13}NO_8$ : C, 50.16; H, 4.21; N, 4.50. Found: C, 50.26; H, 4.28; N, 4.46.

#### 6-(Trifluoroacetylamino)safrole (**15**).

A solution of 2.32 g (13.1 mmoles) of **14** [13] and 1.20 g (15 mmoles) of dry pyridine in 20 ml of ether was cooled in an ice bath and treated dropwise with 3.15 g (15 mmoles) of trifluoroacetic anhydride. After 1 hour, ice was added and the mixture extracted successively with water, 5% aqueous sodium bicarbonate, 1 molar hydrochloric acid, and saturated aqueous sodium chloride. The ether layer was dried and evaporated to give 2.97 g (83%) of **15** with mp 113.5-115°. Recrystallization from 1-chlorobutane afforded pure **15** with mp 116-118°; ir: 3311 (NH) and 1695  $cm^{-1}$  (CO).

Anal. Calcd. for  $C_{12}H_{10}F_3NO_3$ : C, 52.75; H, 3.69; N, 5.13. Found: C, 52.79; H, 3.67; N, 5.14.

#### 3,4-Methylenedioxy-6-(trifluoroacetylamino)phenylacetaldehyde (**16**).

A solution of 1.09 g of **15** in 20 ml of methanol was treated at -78° with a stream of ozonized air until the effluent gas turned potassium iodide-starch solution blue. Dimethyl sulfide, 4 ml, was added and the mixture allowed to warm to room temperature. After 40 minutes, solvent was removed on a rotating evaporator and the residue stirred with ice water. Filtration afforded 0.98 g (89%) of **16**, mp 90-96° raised to mp 100-102.5° by recrystallization from 50% aqueous methanol; ir: 3236 (NH) and 1712  $cm^{-1}$  (amide CO); tlc (chloroform)  $R_f$  0.34.

Anal. Calcd. for  $C_{11}H_8F_3NO_4$ : C, 48.01; H, 2.93; N, 5.09. Found: C, 47.97; H, 2.87; N, 5.08.

Treatment of **16** with 1,1-dimethylhydrazine gave the dimethylhydrazone as needles from ligroin, mp 128-129°; ir: 3195 (NH) and 1712  $cm^{-1}$  (CO); tlc (chloroform):  $R_f$  0.61.

Anal. Calcd. for  $C_{13}H_{14}F_3N_3O_3$ : C, 49.20; H, 4.45; N, 13.24. Found: C, 49.17; H, 4.46; N, 13.16.

#### 3,4-Carbonyldioxyacinnamic Acid (**6**).

In a 250 ml flask equipped with oil bath heater and calcium chloride tube were placed 19.2 g (100 mmoles) of **5** and 12.8 g (350 mmoles) of phosphorus pentachloride. The solid were thoroughly mixed then kept at 105° [15] for 18.5 hours. Volatile byproducts were removed on a rotating evaporator at 100° (20 mm) and the residue treated with 60 ml of 97% formic acid. When gas evolution ceased, the solid was filtered and washed with cold formic acid, acetic acid, and ligroin. The tan powder was dried *in vacuo* over calcium chloride to give 10.4 g (51%) of crude **6** with mp 250-260°. Two recrystallizations from acetic acid [16] followed by sublimation at 140° (0.001 mm) gave an analytical sample, mp 260-261° dec (lit [17 a-b] mp 238-240° dec); ir: 1851 and 1818 (cyclic carbonate CO) and 1681  $cm^{-1}$  (carboxyl CO).

Anal. Calcd. for  $C_{10}H_8O_5$ : C, 58.26; H, 2.93. Found: C, 58.15; H, 2.91.

Alkaline hydrolysis of **6** followed by acidification and ether extraction of the product gave yellowish crystals of caffeic acid with mp 224° dec (lit [18] mp 223-225° dec). The infrared spectrum was essentially identical to a published [19] spectrum for caffeic acid.

#### 3,4-Carbonyldioxy-6-nitrocinnamic Acid (**7b**).

To a mechanically stirred solution of 9.0 g of **6** in 36 ml of concen-

trated sulfuric acid was added 17 ml of 4:1 v/v concentrated sulfuric acid-white fuming 90% nitric acid in small portions during 30 minutes at 0-10°. The mixture was poured onto ice with rapid stirring and the solid immediately filtered, washed extensively with ice water and dried over calcium chloride *in vacuo*. Rapid workup and drying was essential. The light yellow product, mp 190-194°, weighed 9.72 g (88%). Recrystallization from xylene followed by sublimation at 175° (0.001 mm) afforded pure **7b** with mp 204-207° dec; ir: 1851 and 1818 (cyclic carbonate CO) and 1681  $cm^{-1}$  (carboxyl CO); vivid permanganate-like color with aqueous 1 molar potassium hydroxide.

Anal. Calcd. for  $C_{10}H_7NO_7$ : C, 47.82; H, 2.01; N, 5.58. Found: C, 47.74; H, 1.85; N, 5.55.

#### 6-Amino-3,4-carbonyldioxyacinnamic Acid (**8b**).

To a solution of 2.26 g (10 mmoles) of stannous chloride dihydrate in 6 ml of concentrated hydrochloric acid was added 0.502 g (2 mmoles) of **7b** and the mixture stirred at 24-25° for 70 minutes. Solid **7b** was replaced by solid **8b** and complete solution did not occur during the reaction. After 30 minutes in an ice bath, the solid was filtered and washed successively with cold concentrated hydrochloric acid, acetic acid, and ligroin. The dry product weighed 0.518 g (68%) and consisted of the hydrochloride of **8b**; mp 214° dec; ir: 2632 ( $-NH_3^+$ ), 1808 (cyclic carbonate CO) and 1695  $cm^{-1}$  (carboxyl CO).

Sublimation of the hydrochloride at 185° (0.001 mm) gave a bright yellow sublimate, presumably the zwitterion of **8b**, with mp 222-224° dec; ir: 3497, 3413, 2674, 2538 ( $-NH_3^+$ ) and 1842 and 1818  $cm^{-1}$  (cyclic carbonate CO).

Anal. Calcd. for  $C_{10}H_7NO_5$ : C, 54.31; H, 3.19; N, 6.33. Found: C, 54.26; H, 3.16; N, 6.38.

#### 6-Azido-3,4-carbonyldioxyacinnamic Acid (**10b**).

To a mixture of 15 ml of acetic acid-acetic anhydride [20] and 0.920 g (7.2 mmoles) of nitrosylsulfuric acid [21] was added 1.04 g (4 mmoles) of the hydrochloride of **8b**. The temperature was kept between 20 and 35° with an ice bath. After 30 minutes, solid sodium azide, 1.5 g (23 mmoles) was added in small portions. The temperature rose to 45° and was brought back to 25° with an ice bath. The mixture was stirred at 25° for 15 minutes and poured onto 100 ml of ice containing 1 ml of concentrated hydrochloric acid. The solid was filtered, washed with ice water, and dried *in vacuo* over calcium chloride to give 0.97 g (99%) of **10b**, mp 183-185° dec. Recrystallization from ethyl acetate afforded pure **10b** with mp 185.5-186° dec; ir: 2128 (azide) 1852 and 1818 (cyclic carbonate CO) and 1667  $cm^{-1}$  (carboxyl CO).

Anal. Calcd. for  $C_{10}H_5N_4O_5$ : C, 48.59; H, 2.04; N, 17.00. Found: C, 48.63; H, 2.09; N, 16.98.

#### 6-Azido-3,4-methylenedioxyacinnamic Acid (**10a**).

A slurry of 1.03 g (5 mmoles) of **8a** [22] in a mixture of 2 ml of water, 1.2 ml of concentrated hydrochloric acid, 5 ml of acetic acid, and 2 ml of 90% formic acid was treated with a solution of 0.37 g (5 mmoles) of sodium nitrite in small portions during 10 minutes at -5°. After 1 hour, a solution of 0.40 g (6.1 mmoles) of sodium azide in 5 ml of water was added. After 20 minutes the solid was filtered, washed with water, and dried to give 0.95 g (82%) of yellowish-gray **10a** with mp 177-180° dec. Recrystallization from acetic acid and from 1-propanol afforded pure **10a** as ochre crystals with mp 176-180° dec; ir: 2118 (azide) and 1667  $cm^{-1}$  (carboxyl CO).

Anal. Calcd. for  $C_{10}H_7N_3O_4$ : C, 51.50; H, 3.02; N, 18.02. Found: C, 51.69; H, 3.16; N, 17.74.

#### 5,6-Methylenedioxyindole (**2**). (a) From Azido Acid **10a**.

A slow stream of dry nitrogen was bubbled through a solution of 0.25 g of **10a** in 25 ml of *o*-dichlorobenzene maintained at reflux. Gas evolution was monitored by passing the effluent gas through aqueous barium hydroxide and virtually ceased after 4 minutes. Most of the solvent was removed on a rotating evaporator and the residue was chromatographed on a 1.5 × 8 cm column of silica gel. Elution with benzene (10 ml), 1:1 benz-

ene-chloroform (6 ml), and chloroform (25 ml) afforded a fraction which contained a light bluish-olive zone. Evaporation of the solvent afforded 0.115 g (67%) of **2**, mp 105-109.5°. Sublimation at 95° (0.05 mm) gave white crystals of **2** with mp 110-111° (lit [5] mp 110°). A mixture mp of this product with **2** prepared by the literature method showed no depression.

(b) from Nitroaldehyde **12b**.

To a solution of 0.65 g of sodium acetate trihydrate and 1.00 g of sodium dithionite in 10 ml of water was added 0.10 g of finely powdered **12b** and the mixture stirred under nitrogen for 2 days. Filtration afforded 0.05 g (71%) of **2**, mp 106-108°.

(c) From *gem*-Diacetate **13**.

A solution of 76.3 mg of **13** in 2.5 ml of trifluoroacetic acid was stirred with hydrogen in the presence of 27 mg of 10% palladium-charcoal until uptake ceased. The filtered solution was evaporated to a syrup and methanol (2 ml) and concentrated ammonium hydroxide (2 ml) added at 0°. The solution was warmed to 25° for 30 minutes and kept at reflux for 5 minutes. Evaporation of the solvent gave 22 mg (51%) of **2**, mp 95-99°. Sublimation raised the melting point to 106-109°.

(d) From Trifluoroacetylaldehyde **16**.

A solution of 0.642 g of **16** in 20 ml of methanol was treated with 1.28 g of diethylenetriamine. After 20 hours at 30° the solvent was evaporated and the residue taken up in ether. The ether solution was washed successively with 1.2 molar sodium hydroxide, 1 molar hydrochloric acid, and saturated aqueous sodium chloride. Evaporation of the ether afforded 0.29 g (86%) of **2**, mp 106-108.5°.

TLC of **2**.

Each of the products **2a-d** had the same  $R_f$  value of 0.6 (benzene). Visualization of the spots with iodine fumes gave intense, permanent greenish-black spots. The Ehrlich reagent (prepared by dissolving 0.5 g of *p*-dimethylaminobenzaldehyde in 5 ml of acetic acid and adding 5 ml of 85% phosphoric acid) also was usable and gave red spots which rapidly became green-black on heating.

5,6-Carbonyldioxyindole (**4**).

In a 25 ml pear-shaped flask equipped with air condenser, nitrogen bubbler, gas exit tube (all flame dried) and oil bath were placed 0.100 g of **10b**, 0.53 g of copper powder, and 20 ml of *o*-dichlorobenzene (dried by distillation). A slow stream of nitrogen was bubbled through the mixture maintained at 180° by the oil bath. Carbon dioxide evolution was monitored by bubbling the exit gases through aqueous barium hydroxide and became negligible after 35 minutes. After a total reaction time of 50 minutes, the mixture was cooled to 70°, filtered, and the brown filtrate evaporated on a rotating evaporator at 75° (2.0 mm). The residue was stirred with petroleum ether and filtered to give 57 mg (80%) of crude **4**. Sublimation at 150° (0.02 mm) afforded 45 mg of pale yellow powder, mp 176.5-180.5°. Further recrystallization of similar material from 50% aqueous acetic acid and sublimation gave analytically pure **4** with mp 182-183°; ir: 3333 (NH), 1818 and 1786 (cyclic carbonate CO), 1456, 1328, 1266, 1208, 1160, 1139, 1042, 967, 891, 870, 820, 766, 751, 720, and 705  $\text{cm}^{-1}$ ; tlc  $R_f$ , 0.68 (7:2 carbon tetrachloride-pyridine), 0.64 (dichloromethane), 0.69 (8:3 toluene-acetic acid); intense brown-black spots were obtained on the tlc plates by first exposing them to ammonia fumes then iodine vapor.

Compound **4** gives a red color with Ehrlich reagent. With 1 molar aqueous potassium hydroxide, purple solutions were obtained which rapidly turned brown and eventually deposited brown-black solids. With aqueous barium hydroxide, **4** gave an immediate white precipitate of barium carbonate and a purple solution which became brown and deposited solids as with other bases. A micro sample of **4**, recrystallized from boiling water, was examined by tlc and shown to be unchanged **4**. Longer heating with water hydrolyzes the cyclic carbonate ring (see beyond).

*Anal.* Calcd. for  $\text{C}_9\text{H}_7\text{NO}_3$ : C, 61.72; H, 2.88; N, 8.00. Found: C, 61.64; H, 2.77; N, 7.95.

Attempted Synthesis of **4** from **2**.

A mixture of 161 mg (1 mmole) of **2** and 416 mg (2 mmole) of phosphorus pentachloride was heated to 110° for 1 hour with frequent stirring. Treatment of the reaction mixture with formic acid gave only a greenish-black tar from which no **4** could be isolated.

5,6-Dihydroxyindole (**1**).

A mixture of 10 mg of **4** and 0.2 ml of water was kept at 100° for 1 hour with frequent stirring. The solid slowly dissolved with gas evolution. Lyophilization of the water and sublimation of the residue at 125° (0.05 mm) afforded 1.3 mg (15%) of white solid, mp 140-142° dec (lit mp 140° dec [11] [23], 138-139° dec [24], 143-144° dec [25]); tlc,  $R_f$ , 0.35 (7:2 carbon tetrachloride-pyridine) (lit [25]  $R_f$ , 0.28); green color [11] with ferric chloride in ethanol. This experiment was carried out primarily to verify the structure of **4** and was not optimized for yield.

Acknowledgement.

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