

# PATENT SPECIFICATION

(11) **1 600 663**

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## (54) HETEROCYCLYL CARBOXYLBENZOIC ACIDS

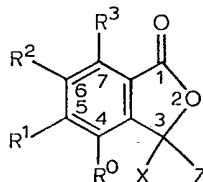
(71) We, **STERLING DRUG INC.**, a corporation organised under the laws of the State of Delaware, United States of America, of 90 Park Avenue, New York, State of New York, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The invention relates to substituted 2 - (indolylcarbonyl)benzoic acids and 2 - (pyrrolylcarbonyl)benzoic acids.

In the Complete Specification of our co-pending Application No. 6228/78, (Serial No. 1600662) out of which the present application is divided, there are described and claimed 3 - aryl - 3 - heteroarylphthalides and 3,3 - bis(heteroaryl)phthalides useful as color precursors, particularly in the art of carbonless duplicating as, for example, in pressure-sensitive systems, in thermal marking systems and in hectographic or spirit-reproducing copying systems.

The compounds of the present invention are useful as intermediates in the preparation of these phthalide color precursors.

The color precursors disclosed in our aforementioned. Application No. 6228/78 Serial No. 1600662 are of the formula:

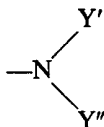


Formula I

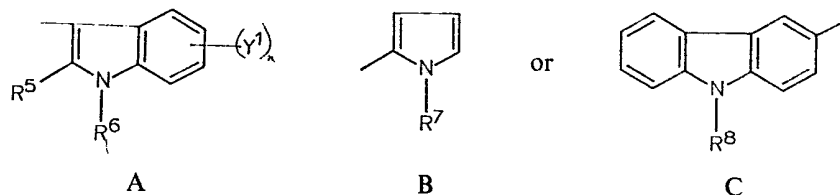
wherein R<sup>0</sup>, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> each represent hydrogen or halo, or when R<sup>0</sup>, R<sup>3</sup> and one of R<sup>1</sup> and R<sup>2</sup> are each hydrogen, the other of R<sup>1</sup> and R<sup>2</sup> represents nitro, amino, acetamido, dialkyl-amino wherein alkyl is non-tertiary C<sub>1</sub> to C<sub>4</sub> alkyl or



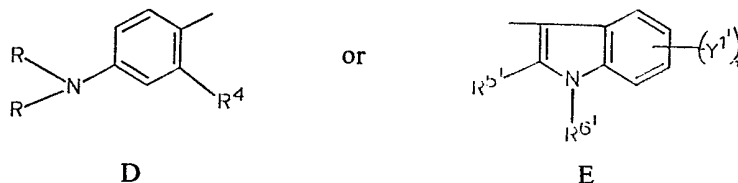
in which B represents —OY or



wherein Y is hydrogen, an alkali metal cation, an ammonium cation, a C<sub>1</sub> to C<sub>18</sub> mono-, di- or trialkylammonium cation, C<sub>1</sub> to C<sub>18</sub> alkyl, C<sub>2</sub> to C<sub>18</sub> alkenyl, benzyl or benzyl substituted in the benzene ring thereof by C<sub>1</sub> to C<sub>12</sub> alkyl, halo or C<sub>1</sub> to C<sub>8</sub> alkoxy; Y' is hydrogen or C<sub>1</sub> to C<sub>18</sub> alkyl; Y'' is hydrogen, C<sub>1</sub> to C<sub>18</sub> alkyl or C<sub>4</sub> to C<sub>12</sub> N,N-dialkylaminoalkyl; X represents a monovalent radical having the formula



Z represents a monovalent radical having the formula

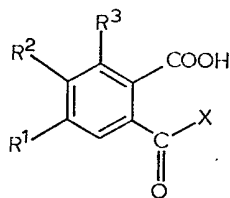


where, in the above, R represents non-tertiary C<sub>1</sub> to C<sub>4</sub> alkyl, benzyl or benzyl substituted in the benzene ring by one or two of halo or C<sub>1</sub> to C<sub>3</sub> alkyl, when X has the Formula B or C, R<sup>4</sup> represents acetamido, dialkylamino in which alkyl is non-tertiary C<sub>1</sub> to C<sub>4</sub> alkyl, and when one of R<sup>1</sup> or R<sup>2</sup> represents any of said carboxy or said carbonyl substituents, R<sup>4</sup> further represents hydrogen, C<sub>1</sub> to C<sub>3</sub> alkyl, C<sub>1</sub> to C<sub>4</sub> alkoxy or halo, and when X has the Formula A, one of R<sup>1</sup> and R<sup>2</sup> must represent one of said carboxy or said carbonyl groups and R<sub>4</sub> represents hydrogen, acetamido, dialkylamino in which alkyl is non-tertiary C<sub>1</sub> to C<sub>4</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkyl, C<sub>1</sub> to C<sub>4</sub> alkoxy or halo, R<sup>5</sup> and R<sup>5'</sup> represent hydrogen, C<sub>1</sub> to C<sub>3</sub> alkyl or phenyl, R<sup>6</sup> and R<sup>6'</sup> represent hydrogen, C<sub>1</sub> to C<sub>18</sub> alkyl, C<sub>2</sub> to C<sub>4</sub> alkenyl, benzyl or benzyl substituted in the benzene ring by one or two of halo or C<sub>1</sub> to C<sub>3</sub> alkyl, R<sup>7</sup> and R<sup>8</sup> represent hydrogen, C<sub>1</sub> to C<sub>3</sub> alkyl or phenyl, and Y<sup>1</sup> and Y<sup>1'</sup> each represent hydrogen or C<sub>1</sub> to C<sub>3</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkoxy, halo or nitro substituents in the benzenoid portion of the indolyl radical, and n is 1 or 2, with the provisos (i) that X and Z can both simultaneously represent mono-valent indolyl moieties only when one of R<sup>1</sup> and R<sup>2</sup> represent said



and (ii) X represents a pyrrolyl or a carbazolyl moiety only when Z represents a 2-R<sup>4</sup>-4-N-(R)<sub>2</sub>-phenyl moiety. The Y<sup>1</sup> and Y<sup>2</sup> substituents referred to throughout are preferably at the 5- or 6-position of the indole ring.

The novel 2-(X-carbonyl)-3-R<sup>0</sup>-4-R<sup>1</sup>-5-R<sup>2</sup>-6-R<sup>3</sup>-benzoic acids which are the subject of the present application have the formula



Formula VII

wherein R<sup>0</sup>, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> each represent hydrogen or halo, or when R<sup>0</sup>, R<sup>3</sup> and one of R<sup>1</sup> and R<sup>2</sup> are each hydrogen, the other of R<sup>1</sup> and R<sup>2</sup> represents amino or carboxy; X represents a monovalent radical having the Formula A or B above in

which R<sup>5</sup> represents hydrogen, C<sub>1</sub> to C<sub>3</sub> alkyl or phenyl, R<sup>6</sup> represents C<sub>4</sub> to C<sub>18</sub> alkyl, C<sub>2</sub> to C<sub>4</sub> alkenyl, benzyl or benzyl substituted in the benzene ring by one or two of halo or C<sub>1</sub> to C<sub>3</sub> alkyl or represents hydrogen or C<sub>1</sub> to C<sub>3</sub> alkyl only when Y<sup>1</sup> is other than hydrogen and/or when one of R<sup>1</sup> and R<sup>2</sup> is amino or carboxy; R<sup>7</sup> represents hydrogen, C<sub>1</sub> to C<sub>3</sub> alkyl or phenyl; and Y<sup>1</sup> represents hydrogen or C<sub>1</sub> to C<sub>3</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkoxy, halo or nitro in the benzenoid portion of the indolyl radical, and n is 1 or 2. The compounds of Formula VII when X are radicals A and B are referred to as Formulas VIII and IX, respectively.

As used herein the term "halo" includes chloro, fluoro, bromo and iodo. Chloro is the preferred halo substituent because of the relatively low cost and ease of preparation of the required chloro-substituted intermediates and because the other halogens offer no particular advantages over chloro. However the other above-named halo substituents are also satisfactory.

The term "C<sub>1</sub> to C<sub>3</sub> alkoxy" denotes saturated, acyclic groups which may be straight or branched as exemplified by methoxy, ethoxy, propoxy and isopropoxy.

As used herein the terms "C<sub>1</sub> to C<sub>3</sub> alkyl", and "C<sub>4</sub> to C<sub>18</sub> alkyl" denote saturated monovalent straight or branched aliphatic hydrocarbon radicals including methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, amyl, 1-methylbutyl, 3-methylbutyl, hexyl, isohexyl, heptyl, isoheptyl, octyl, isooctyl, 2-ethylhexyl, nonyl, 3-ethylheptyl, n-decyl, n-undecyl, n-dodecyl, n-tridecyl, n-tetradecyl, n-pentadecyl, n-hexadecyl, n-heptadecyl, n-octadecyl, 1,3,5-trimethylhexyl, 1,5-dimethyl-4-ethylhexyl, 5-methyl-2-butyl-hexyl, 2-propylnonyl, 2-butyloctyl, 2-pentylnonyl and 1,2-dimethylhexadecyl.

As used herein, the term "C<sub>2</sub> to C<sub>4</sub> alkenyl" means a monovalent aliphatic radical possessing a single double bond, for example, ethenyl (or vinyl), 2-propenyl (or allyl), 1-methyl-ethenyl (or isopropenyl), 2-methyl-2-propenyl, 2-methyl-1-propenyl, 2-butenyl and 3-butenyl.

The 3-X-3-Z-4-R<sup>0</sup>-5-R<sup>1</sup>-6-R<sup>2</sup>-7-R<sup>3</sup>-phthalides of Formula I wherein R<sup>0</sup>, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> each represent hydrogen or halo and when R<sup>0</sup>, R<sup>3</sup> and one of R<sup>1</sup> and R<sup>2</sup> are each hydrogen and the other represents nitro, dialkylamino or carboxy are obtained by interacting approximately an equimolar quantity of the appropriate 2-(X-carbonyl)-3-R<sup>0</sup>-4-R<sup>1</sup>-5-R<sup>2</sup>-6-R<sup>3</sup>-benzoic acid of the Formula VII with the appropriate 3-R<sup>4</sup>-N,N-(R)<sub>2</sub>-aniline or a 1-R<sup>6</sup>-2-R<sup>5</sup>-Y<sup>1</sup>-indole. The reaction is conveniently carried out in the presence of an anhydride of an alkanolic acid having from 2 to 5 carbon atoms, for example, acetic anhydride at a temperature in the range of 10 to 140°C. for from approximately thirty minutes to eighteen hours.

The 3-X-3-Z-5/6-acetamidophthalide according to Formula I can be conveniently obtained by interacting the appropriate compound of Formula VII, wherein one of R<sup>1</sup> and R<sup>2</sup> is amino and the other and each of R<sup>0</sup> and R<sup>3</sup> are hydrogens, with approximately an equimolar quantity of an appropriate 3-R<sup>4</sup>-N,N-(R)<sub>2</sub>-aniline or a 1-R<sup>6</sup>-2-R<sup>5</sup>-Y<sup>1</sup>-indole in the presence of at least two molecular proportions of acetic anhydride. Both these reactions are described and claimed in our forementioned Application No. 6228/78. Serial No. 1600662.

The novel 2-X-carbonyl-3-R<sup>0</sup>-4-R<sup>1</sup>-5-R<sup>2</sup>-6-R<sup>3</sup>-benzoic acids of Formula VII are prepared by interacting a 3-R<sup>0</sup>-4-R<sup>1</sup>-5-R<sup>2</sup>-6-R<sup>3</sup>-phthalic anhydride with approximately one molecular proportion of a 1-R<sup>6</sup>-2-R<sup>5</sup>-Y<sup>1</sup>-indole or a 1-R<sup>7</sup>-pyrrole, wherein R<sup>0</sup>, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and Y<sup>1</sup> each have the same meanings given in relation to Formula VII in the presence of a Lewis acid, for example, aluminum chloride or zinc chloride, and usually with a diluent such as benzene, toluene, xylene, chlorobenzene, 1,2-dichloro-ethane or *o*-dichlorobenzene generally at a temperature of 0 to 150°C. The reaction is conveniently carried out in toluene in the presence of aluminum chloride at 0 to 25°C. Alternatively, the more reactive indoles can be interacted in the absence of a Lewis acid by simply heating the reactants together in an inert solvent at 80 to 150°C. The 2-(X-carbonyl)-3-R<sup>0</sup>-4-R<sup>1</sup>-5-R<sup>2</sup>-6-R<sup>3</sup>-benzoic acids in which Lewis acids are used in their preparation are isolated by adding water to the reaction mixture or the reaction mixture to water or dilute mineral acid, for example, hydrochloric acid and subsequently separating the organic layer. The product is extracted from the organic layer with a dilute aqueous alkali solution and precipitated by the addition of a mineral acid, for example, hydrochloric acid. The benzoic acid is collected by filtration and may be purified by conventional means but is generally dried and used as is. Alternatively, in the case where the more reactive indoles are utilized, it is preferable not to use a Lewis acid and the 2-(X-carbonyl)-3-R<sup>0</sup>-4-R<sup>1</sup>-5-R<sup>2</sup>-6-R<sup>3</sup>-benzoic acids are obtained

by cooling the reaction mixture to ambient temperature and collecting the product by filtration. The product once isolated can be purified by conventional means but preferably the benzoic acid is dried and used as is.

5 The 2 - (X - carbonyl) - 5/6 - aminobenzoic acids of Formula VII are  
 5 obtained by reducing the corresponding 2 - (X - carbonyl) - 5/6 - nitrobenzoic  
 acid. The reduction is conveniently carried out in an acidic medium, for example,  
 hydrochloric acid using a metal salt reducing agent, for example, stannous  
 chloride at a temperature in the range of 0 to 80°C., but preferably at a  
 10 temperature in the range of 50—80°C. The desired benzoic acid is collected by  
 10 filtration and purified if desired by conventional means but preferably it is dried  
 and used as is.

It will, of course, be appreciated that reaction of an unsymmetrically  
 substituted phthalic anhydride with an indole or pyrrole can produce isomers or a  
 mixture of isomers of 2-(heteroarylcarbonyl)benzoic acids. For example, reaction  
 15 of a 4-substituted phthalic anhydride with an indole or pyrrole can produce either a  
 15 4- or 5-substituted 2-(heteroarylcarbonyl)benzoic acid or a mixture thereof.  
 Similarly a 3- substituted phthalic anhydride can produce either a 3- or a 6-  
 substituted 2-(heteroarylcarbonyl)benzoic acid or a mixture of these. The mixtures  
 20 of isomeric 2-(heteroarylcarbonyl) benzoic acids can be separated by conventional  
 20 means such as fractional crystallization or chromatography. Alternatively, the  
 isomeric mixtures can be reacted directly with appropriate 3 - R<sup>4</sup> - N,N - (R)<sub>2</sub> -  
 anilines or 1-R<sup>6'</sup>-2-R<sup>5'</sup>-5/6-Y<sup>1'</sup>-indoles to produce isomeric mixtures of phthalides  
 of Formula I. Thus, reaction of a mixture of 4- and 5-substituted 2-  
 25 (heteroarylcarbonyl)benzoic acids with a 3 - R<sup>4</sup> - N,N - (R)<sub>2</sub> - aniline or a 1-R<sup>6'</sup> -  
 25 2 - R<sup>5'</sup> - 5/6 - Y<sup>1'</sup> - indole will produce a mixture of 5- and 6-substituted  
 phthalides. The mixtures of phthalides can, if desired, be separated by conventional  
 means or simply and preferably used as mixtures in the practice of this invention.  
 Throughout this application where the possibility of different isomeric products  
 30 being formed is present, the nomenclature 4/5, 5/6 and so forth is adopted meaning  
 30 the product obtained or claimed is a mixture of the isomers.

Indoles, the substituted indoles, pyrrole and the substituted pyrroles required  
 as intermediates for the preparation of the carbonylbenzoic acid intermediates of  
 Formula VII, VIII and IX and for the final products of Formula I, form an old and  
 well-known class of compounds which are readily obtained by conventional  
 35 procedures well known in the art. The following compounds are exemplary of  
 35 indoles, pyrroles and carbazoles useful in the practice of this invention: indole, 1-  
 methylindole, 2-methylindole, 1,2-dimethylindole, 1 - ethyl - 2 - methylindole, 2-  
 phenylindole, 1 - propyl - 2 - methylindole, 1 - benzyl - 2 - methylindole, 1 -  
 40 butyl - 2 - methylindole, 1 - octyl - 2 - methylindole, 2 - ethyl - 5 - methylindole,  
 40 1 - benzyl - 5 - fluoroindole, 1 - methyl - 6 - nitroindole, 5 - methoxy - 1 -  
 butylindole, 1 - allyl - 2 - methylindole, 1,2 - dimethyl - 6 - nitroindole, 1 - (4 -  
 chlorobenzyl) - 2 - methyl - 5 - nitroindole, 2-ethylindole, 2 - ethyl - 1 -  
 methylindole, 1-isopropylindole, 2-isopropylindole, 1 - methyl - 5 - bromo - 6 -  
 45 nitroindole, 2,5,6 - trimethylindole, 1 - isobutyl - 2 - methylindole, 6 - bromo -  
 45 2 - methylindole, 1-hexylindole, 1 - (2,5 - dimethylbenzyl) - 2 - methylindole, 2-  
 propylindole, 6 - chloro - 2 - phenylindole, 1 - (2 - ethylhexyl) - 2 -  
 methylindole, 1 - (2,6 - dichlorobenzyl) - 2 - methylindole, 1 - vinyl - 2 -  
 methylindole, 2 - ethyl - 6 - methylindole, 6 - fluoro - 1 - benzylindole, 1 - (4 -  
 50 bromobenzyl) - 2 - isopropylindole, 1 - (3 - chlorobenzyl) - 2 - ethylindole, 5 -  
 50 chloro - 1 - benzylindole, 1 - (2 - fluorobenzyl) - 2 - methylindole, 5 - iodo - 1 -  
 (1 - methylhexyl) - indole, 5,6 - dimethoxyindole, 1 - (2 - methylbenzyl) - 2 -  
 methylindole, 5,6 - dichloro - 2 - phenylindole, 1-isoamylindole, 1 - [3 - (2 -  
 methyl) - 1 - propenyl] - 2 - methoxyindole, pyrrole, N-methylpyrrole, N-  
 ethylpyrrole, N-propylpyrrole, N-isopropylpyrrole and N-phenylpyrrole.

55 The molecular structures of the compounds of this invention were assigned on  
 55 the basis of the modes of synthesis, elemental analysis and study of their infrared,  
 nuclear magnetic resonance, and mass spectra.

The following examples will further illustrate the invention without, however,  
 limiting it thereto.

60 Example 1 60

To a stirred suspension of 22.5 g (0.15 mole) of phthalic anhydride and 61.0 g  
 (0.30 mole) of 77.5 percent active 1 - ethyl - 2 - methylindole in 120 ml of ethylene  
 dichloride chilled to 0 to 5°C by means of an ice bath, there was added in small  
 portions 32.0 g (0.24 mole) of aluminum chloride. The mixture was maintained at

0—5°C for an additional 15 minutes, allowed to warm to room temperature and stirred overnight. Then, 240 ml of water was added to the reaction mixture and the ethylene dichloride layer was separated from the acidic aqueous layer. The organic layer was extracted with 600 ml of 3.5 percent aqueous sodium hydroxide. The alkaline extract was acidified with dilute hydrochloric acid and the separated solid collected, washed with water and dried to obtain 24.0 g of 2 - [(1 - ethyl - 2 - methyl - 3 - indolyl)carbonyl]benzoic acid (Formula VIII: R<sup>0</sup>=R<sup>1</sup>=R<sup>2</sup>=R<sup>3</sup>=Y<sup>1</sup>=H; R<sup>5</sup>=CH<sub>3</sub>; R<sup>6</sup>=CH<sub>2</sub>CH<sub>3</sub>), a slightly pink solid having a melting point of 184—185°C.

#### Example 2

To a stirred suspension of 9.66 g (0.017 mole) of tetrachlorophthalic anhydride and 13.5 g (0.034 mole) of 80 percent active 1 - ethyl - 2 - methylindole in 30 ml of benzene maintained at 0—5°C by means of an ice bath, 10.6 g (0.079 mole) of aluminum chloride was added in small increments. The reaction mixture was then maintained at 0 to 5°C for an additional twenty minutes, allowed to warm to room temperature and stirred overnight. The mixture was transferred to a beaker and triturated successively with hexane, 10 percent hydrochloric acid, and lastly with 5 percent aqueous sodium hydroxide which had been heated to 70°C. The residual oil was filtered, acidified with dilute hydrochloric acid and allowed to stand overnight. On standing, the oil gave way to a solid which was collected by filtration, washed with water and dried to yield 6.8 g of 2 - [(1 - ethyl - 2 - methyl - 3 - indolyl)carbonyl] - 3,4,5,6 - tetrachlorobenzoic acid (Formula VIII: R<sup>0</sup>=R<sup>1</sup>=R<sup>2</sup>=R<sup>3</sup>=Cl; R<sup>5</sup>=CH<sub>3</sub>; R<sup>6</sup>=CH<sub>2</sub>CH<sub>2</sub>; Y<sup>1</sup>=H), an off white solid melting at 214—216°C. Analysis by mass spectrum showed m/e peaks at 443 (M<sup>+</sup>, Cl=35) and 398 (M<sup>+</sup>-COOH).

#### Example 3

A. A solution of 67.2 g (0.4 mole) of 4 - nitrophthalic anhydride and 63.0 g (0.32 mole) of 80.6 percent active 1 - ethyl - 2 - methylindole in 50 ml of ethylene dichloride was heated at reflux for two hours. The reaction mixture was then allowed to cool to room temperature. The yellow precipitate which separated was collected by filtration, washed with fresh ethylenedichloride and dried to obtain 64.5 g of 2 - [(1 - ethyl - 2 - methyl - 3 - indolyl)carbonyl] - 5 - nitrobenzoic acid having a melting point of 203—204°C.

B. To a solution of 7.04 g (0.02 mole) of 2 - [(1 - ethyl - 2 - methyl - 3 - indolyl)carbonyl] - 5 - nitrobenzoic acid, prepared as described in part A of this example, in 70 ml of concentrated hydrochloric acid, there was added 13.5 g (0.06 mole) of stannous chloride dihydrate at such a rate as to allow the reaction to exotherm to 55°C. The temperature was maintained at 55°C for an additional one-half hour. The reaction was then cooled to room temperature and the pH adjusted to six by the addition of 10 percent aqueous sodium hydroxide solution. The red precipitate thus formed was filtered off and extracted into acetone. The acetone solution was evaporated and the paste-like residue was slurried in diethylether and then the solid was collected by filtration to obtain 3.5 g of 2 - [(1 - ethyl - 2 - methyl - 3 - indolyl) - carbonyl] - 5 - aminobenzoic acid (Formula VIII: R<sup>3</sup>=R<sup>2</sup>=R<sup>0</sup>=Y<sup>1</sup>=H; R<sup>1</sup>=NH<sub>2</sub>; R<sup>5</sup>=CH<sub>3</sub>; R<sup>6</sup>=CH<sub>2</sub>CH<sub>3</sub>), a red solid which melted at 187—189°C.

#### Example 4

Following the procedure described in Example 1, 7.4 g (0.05 mole) of phthalic anhydride, 16.0 g (0.07 mole) of 79 percent active 1 - n - butyl - 2 - methylindole and 13.3 g (.01 mole) of aluminum chloride were interacted in 50 ml of benzene to obtain 2 - [(1 - n - butyl - 2 - methyl - 3 - indolyl)carbonyl]benzoic acid (Formula VIII: R<sup>0</sup>=R<sup>1</sup>=R<sup>2</sup>=R<sup>3</sup>=Y<sup>1</sup>=H; R<sup>5</sup>=CH<sub>3</sub>; R<sup>6</sup>=(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>) a pale pink solid melting over the range 88—92°C. The nuclear magnetic resonance spectrum was consistent with the structure. Infrared maxima were recorded at 1720 cm<sup>-1</sup> (C=O; s) and 1700 cm<sup>-1</sup> (C=O; s).

#### Example 5

In a manner similar to that described in Example 1 hereinabove, 7.4 g (0.05 mole) of phthalic anhydride, 16.0 g (0.053 mole) of 76.5 percent active 1 - n - octyl - 2 - methyl - indole, and 13.3 g (0.1 mole) of aluminum chloride were interacted in 50 ml of benzene to obtain 6.9 g of 2 - [(1 - n - octyl - 2 - methyl - 3 - indolyl)carbonyl]benzoic acid (Formula VIII: R<sup>0</sup>=R<sup>1</sup>=R<sup>2</sup>=R<sup>3</sup>=Y<sup>1</sup>=H; R<sup>5</sup>=CH<sub>3</sub>; R<sup>6</sup>=(CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), as a pink-colored powder which melted at 121—123°C. The

nuclear magnetic spectrum was in agreement with the structure and a significant maxima occurred at  $1717\text{ cm}^{-1}$  (C=O; s).

#### Example 6

Proceeding in a manner similar to that described in Example 2, 14.3 g (0.05 mole) of tetrachlorophthalic anhydride, 16.0 g (0.07 mole) of 76 percent active 1 - *n* - butyl - 2 - methylindole and 13.3 g (0.10 mole) of aluminum chloride were interacted in 100 ml of benzene. The reaction mixture was drowned in 200 ml of five percent hydrochloric acid with stirring. The solid which formed was collected by filtration, washed with water and dried to obtain 2 - *[(1 - n - butyl - 2 - methyl - 3 - indolyl)carbonyl] - 3,4,5,6 - tetrachlorobenzoic acid* (Formula VIII:  $R^0=R^1=R^2=R^3=Y^1=H$ ;  $R^5=CH_3$ ;  $R^6=(CH_2)_3CH_3$ ), a pale yellow solid melting at  $162\text{--}164^\circ\text{C}$ . The nuclear magnetic resonance spectrum was in accord with the structure.

#### Example 7

Proceeding in the same manner as that described in Example 6 above, 14.3 g (0.05 mole) of tetrachloro-phthalic anhydride, 16.0 g (0.052 mole) of 76.5 percent active 1 - *n* - octyl - 2 - methylindole and 13.3 g (0.10 mole) of aluminum chloride were interacted to obtain 2 - *[(1 - n - octyl - 2 - methyl - 3 - indolyl)carbonyl] - 3,4,5,6 - tetrachlorobenzoic acid* (Formula VIII:  $R^0=R^1=R^2=R^3=Cl$ ;  $R^5=CH_3$ ;  $R^6=(CH_2)_7CH_3$ ;  $Y^1=H$ ), a pale orange solid melting at  $132\text{--}134^\circ\text{C}$ . The infrared spectrum, showing a maximum at  $1745\text{ cm}^{-1}$  (C=O; s) and the nuclear magnetic resonance spectrum was in accord with the structure.

#### Example 8

A suspension of 14.8 g (0.10 mole) of phthalic anhydride, 10.5 g (0.05 mole) of 2-phenylindole and 82 ml of xylene was heated to  $110^\circ\text{C}$  briefly, cooled to and maintained at  $95^\circ\text{C}$  for approximately two hours. The solution was cooled to ambient temperature and the solid which separated was collected by filtration and dried to obtain 10.6 g of 2 - *[(2 - phenyl - 3 - indolyl)carbonyl]benzoic acid* (Formula VIII:  $R^0=R^1=R^2=R^3=R^6=Y^1=H$ ;  $R^5=C_6H_5$ ) which melted at  $106\text{--}107^\circ\text{C}$  and had a nuclear magnetic resonance spectrum consistent with the assigned structure.

#### Example 9

Proceeding in a manner similar to Example 8, but substituting 2-methylindole for 2-phenylindole, there was obtained 2 - *[(2 - methyl - 3 - indolyl)carbonyl]benzoic acid* (Formula VIII:  $R^0=R^1=R^2=R^3=R^6=Y^1=H$ ;  $R^5=CH_3$ ), as pale pink-colored crystals melting at  $198\text{--}200^\circ\text{C}$ .

#### Example 10

A mixture of 5.0 g (0.03 mole) of 5 - methoxy - 2 - methyl - indole and 4.6 g (0.03 mole) of phthalic anhydride in 25 ml of ethylene dichloride was refluxed for ten hours, cooled to room temperature and the separated solid was collected by filtration and dried to obtain 2 - *[(2 - methyl - 5 - methoxy - 3 - indolyl)carbonyl] - benzoic acid* (Formula VIII:  $R^0=R^1=R^2=R^3=R^6=H$ ;  $R^5=CH_3$ ;  $Y^1=OCH_3$ ), as a pale pink-colored solid which decomposed at  $203\text{--}204^\circ\text{C}$ . The nuclear magnetic resonance and infrared spectra were consistent with the assigned structure.

#### Example 11

A mixture of 5.0 g (0.034 mole) of phthalic anhydride and 5.0 g (0.034 mole) of 2,5 - dimethylindole in 30 ml of ethylenedichloride was refluxed for 20 hours, cooled and the separated solid filtered off and dried to obtain 3.8 g of 2 - *[(2,5 - dimethyl - 3 - indolyl)carbonyl]benzoic acid* (Formula VIII:  $R^0=R^1=R^2=R^3=R^6=H$ ;  $R^5=CH_3$ ;  $Y^1=CH_3$ ) as a pink-colored solid melting at  $198\text{--}200^\circ\text{C}$ .

#### Example 12

To a mixture of 2.96 g (0.02 mole) of phthalic anhydride and 5.72 g (0.04 mole) of *n*-phenylpyrrole in 50 ml of chlorobenzene, maintained at  $0\text{--}5^\circ\text{C}$ . in an ice bath, 810 g (0.06 mole) of aluminum chloride was added in small portions. The reaction mixture was held at  $0\text{--}5^\circ\text{C}$ . for approximately two hours. The reaction was allowed to warm to room temperature and then set aside overnight at ambient temperature. The reaction mixture was poured onto ice and rendered acidic by the addition of 10 percent hydrochloric acid. The chlorobenzene layer was separated

and steam-distilled to remove the chlorobenzene. The residue was extracted with 10 percent aqueous sodium hydroxide, filtered to remove the insolubles and then acidified with dilute hydrochloric acid. The solid which separated was collected by filtration, washed with water and dried to obtain 2 - [(1 - phenyl - 2 - pyrrolyl)carbonyl]benzoic acid (Formula IX:  $R^0=R^1=R^2=R^3=H$ ;  $R^7=C_6H_5$ ) which melted over the range 159—168°C.

#### Example 13

Proceeding in a manner similar to that described in Example 16, 14.8 g (0.1 mole) of phthalic anhydride, 16.2 (0.2 mole) of N - methylpyrrole and 39.0 g (0.3 mole) of aluminum chloride were interacted in 50 ml of chlorobenzene to obtain 2 - [(1 - methyl - 2 - pyrrolyl)carbonyl]benzoic acid (Formula IX:  $R^0=R^1=R^2=R^3=H$ ;  $R^7=CH_3$ ) melting at 165—167°C. A significant infrared absorption maximum appeared at 1710  $cm^{-1}$  (C=O; s).

#### Example 14

A stirred solution of 48.0 g (0.250 mole) of trimellitic anhydride and 45.0 g (0.314 mole) of 1 - ethyl - 2 - methylindole in 350 ml of ethylene dichloride was heated at reflux for a period of approximately two hours, and then allowed to cool to ambient temperature. The solid, which separated, was collected by filtration, washed with 200 ml of ethylene dichloride and dried *in vacuo* at 60°C to obtain 66.0 g of 4/5 - carboxy - 2 - [(1 - ethyl - 2 - methyl - 3 - indolyl)carbonyl]benzoic acid (Formula VIII:  $R^1=R^2=H/COOH$ ;  $R^0=R^3=Y^1=H$ ;  $R^4=CH_3$ ;  $R^6=CH_2CH_3$ ), a yellowish-orange solid melting over the range 198—201°C. Infrared maxima appeared at 1730 (C=O; s) and 1700  $cm^{-1}$  (C=O; vs). The nuclear magnetic resonance spectrum was in agreement with the assigned structure.

#### Example 15

Proceeding in a manner similar to that described in Example 10, 29.6 g (0.20 mole) of phthalic anhydride and 35.2 g (0.20 mole) of 5 - nitro - 2 - methylindole were interacted in 100 ml of ethylene dichloride to obtain 2 - [(2 - methyl - 5 - nitro - 3 - indolyl) - carbonyl]benzoic acid (Formula VIII:  $R^0=R^1=R^2=R^3=R^6=H$ ;  $R^5=CH_3$ ;  $Y^1=5-NO_2$ ), a red brown solid melting at 144—148°C and showing a strong carbonyl absorption maximum at 1700  $cm^{-1}$  in the infrared spectrum.

#### Example 16

Using a procedure similar to the one described in Example 10, 48.0 g (0.25 mole) of trimellitic anhydride and 32.8 g (0.25 mole) of 2-methylindole were interacted in 250 ml of ethylene dichloride to obtain 66.1 g of 4/5 - carboxy - 2 - [(2 - methyl - 3 - indolyl)carbonyl]benzoic acid (Formula VIII:  $R^1=R^2=H/COOH$ ;  $R^0=R^3=R^6=Y^1=H$ ;  $R^5=CH_3$ ) melting at 237—241°C.

#### Example 17

Proceeding in a similar fashion to the one described in Example 13, 28.6 g (0.01 mole) of tetrachlorophthalic anhydride, 16.2 g (0.2 mole) of N-methylpyrrole and 40 g (0.3 mole) of aluminum chloride were interacted in 50 ml of dry chlorobenzene to obtain 2 - [(1 - methyl - 2 - pyrrolyl)carbonyl] - 3,4,5,6 - tetrachloro - benzoic acid (Formula IX:  $R^0=R^1=R^2=R^3=Cl$ ;  $R^7=CH_3$ ) having a melting point of 203—205°C.

#### WHAT WE CLAIM IS:—

1. A compound of the Formula VII (herein) wherein:  $R^0$ ,  $R^1$ ,  $R^2$ , and  $R^3$  each represent hydrogen or halo, or when  $R^0$ ,  $R^3$  and one of  $R^1$  and  $R^2$  are each hydrogen, the other of  $R^1$  and  $R^2$  represents amino or carboxy;

X represents a monovalent radical having the Formula A or B (herein) in which  $R^5$  represents hydrogen,  $C_1$  to  $C_3$  alkyl or phenyl,

$R^6$  represents  $C_4$  to  $C_{18}$  alkyl,  $C_2$  to  $C_4$  alkenyl, benzyl or benzyl substituted in the benzene ring by one or two of halo or  $C_1$  to  $C_3$  alkyl or represents hydrogen or  $C_1$  to  $C_3$  alkyl only when  $Y^1$  is other than hydrogen and/or when one of  $R^1$  and  $R^2$  is amino or carboxy;

$R^7$  represents hydrogen,  $C_1$  to  $C_3$  alkyl or phenyl;  $Y^1$  represents hydrogen or  $C_1$  to  $C_3$  alkyl,  $C_1$  to  $C_3$  alkoxy, halo or nitro in the benzenoid portion of the indole radical, and n is 1 or 2.

2. 2 - [2,5 - Dimethyl - 3 - indolyl]carbonyl]benzoic acid.

3. 2 - [(2 - Methyl - 5 - methoxy - 3 - indolyl)carbonyl]benzoic acid.

4. 2 - [(1 - n - Butyl - 2 - methyl - 3 - indolyl)carbonyl]benzoic acid.

5. 2 - [(1 - *n* - Octyl - 2 - methyl - 3 - indolyl)carbonyl]benzoic acid.
6. 5 - Amino - 2 - [(1 - ethyl - 2 - methyl - 3 - indolyl)carbonyl]benzoic acid.
7. 2 - [(1 - *n* - Butyl - 2 - methyl - 3 - indolyl)carbonyl] - 3,4,5,6 - tetrachlorobenzoic acid.
- 5 8. 2 - [(1 - *n* - Octyl - 2 - methyl - 3 - indolyl)carbonyl] - 3,4,5,6 - tetrachlorobenzoic acid. 5
9. 2 - [(1 - Ethyl - 2 - methyl - 3 - indolyl)carbonyl] - 4/5 - carboxy - benzoic acid.
- 10 10. 2 - [(1 - Methyl - 1H - 2 - pyrrolyl)carbonyl]benzoic acid. 10
11. 2 - [(1 - Phenyl - 1H - 2 - pyrrolyl)carbonyl]benzoic acid. 10
12. 2 - [(1 - Methyl - 1H - 2 - pyrrolyl)carbonyl] - 3,4,5,6 - tetra-chlorobenzoic acid.
13. A compound according to claim 1, in which X has the Formula B (herein).
- 15 14. A process for preparing a compound according to claim 1, wherein R<sup>0</sup>, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> each represent hydrogen or halo, or when R<sup>0</sup>, R<sup>3</sup> and one of R<sup>1</sup> and R<sup>2</sup> are each hydrogen, the other of R<sup>1</sup> and R<sup>2</sup> represents carboxy and R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and Y<sup>1</sup> each have the same respective meanings given in claim 1, which comprises interacting a 3 - R<sup>0</sup> - 4 - R<sup>1</sup> - 5 - R<sup>2</sup> - 6 - R<sup>3</sup> - phthalic anhydride with approximately one molecular proportion of a 1 - R<sup>6</sup> - 2 - R<sup>5</sup> - Y<sup>1</sup> - indole or a 1 - R<sup>7</sup> - pyrrole in the presence of a Lewis acid. 15
- 20 15. A process for preparing a compound according to claim 1, where one of R<sup>1</sup> and R<sup>2</sup> is amino which comprises reducing the corresponding compound of Formula VII wherein one of R<sup>1</sup> and R<sup>2</sup> is nitro. 20
- 25 16. A process for preparing a compound according to claim 1, substantially as herein described with reference to the Examples. 25
17. A compound when prepared by the process according to any one of claims 14 to 16.
18. A compound according to claim 1, substantially as herein described with reference to the Examples.

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