stirred for 24 h. The reaction mixture was treated analogously to Va to yield 0.75 g (69%) IXa with up 203-204°C. The IR spectrum was identical to the spectrum of the sample obtained by method A.

<u>N,N-Diphenylhydrazide of β -chloropropionic acid (IIIc)</u> was obtained analogously to Ia-c from N,N-diphenylhydrazine and β -chloropropionyl chloride in 60% yield, mp 133-135°C (from ethanol). IR spectrum: 3220 (NH), 1665 cm⁻¹ (C=0). Found: C, 65.8; H, 6.0; N, 10.6%. Calculated for C₁₅H₁₅ClN₂O: C, 65.6; H, 5.5; N, 10.2%.

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SYNTHESIS OF 2-ACYLINDOLES FROM α -(N-ISATINYL) KETONES

UDC 547.756'757.07

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2-Acylindoles were synthesized by the recyclization of N-phenacyl- and N-acetonylisatins in alkaline media and the decarboxylation of 2-acylindolyl-3-carboxylic acids or their salts in basic or neutral media.

2-Acylindoles are used as starting compounds for the synthesis of sedatives [1] and the study of their rearrangement to give 3-acylindoles [2]. These compounds, nevertheless, are not readily available despite a number of special or multistep methods for their preparation [1-8].

We have developed a simple general method for the synthesis of 2-acylindoles by the action of alkali on α -(N-isatinyl) ketones [10].* This reaction may be carried out in water or in a mixture of water and an organic solvent. At 60-70°C and 5% NaOH, the reaction is complete in 3-4 h. 2-Aroylindoles are obtained in high yields (Table 1), while 2-acetylindole and 2-acetyl-5-bromoindole are obtained in 29 and 38% yield, respectively. This decrease in yield is the result of an intermolecular aldol-crotonic condensation of 2-acetylindoles. (We did not carry out a special study of this reaction). If the synthesis of 2aroylindoles is carried out in a homogeneous medium (1:1 water-DMF, 5% NaOH), purification of the reaction products is significantly simplified. In this case, the precipitate of analytically pure compound is easily separated from the colored impurities which remain in solution.

The formation of 2-acylindoles involve the opening of the five-membered ring of isatin (I) by the action of alkali, the spontaneous cyclization of N-phenacyl- and N-acetonyl-oaminophenylglyoxylic acids (II) into 2-acylindolyl-3-carboxylic acids (III), and the decarboxylation of III without their separation from the reaction mixture:



*After the publication of our work [10, 11, 14-16], the brief communication of Black and Wong [9] appeared on the same subject.

Institute of Chemistry, Academy of Sciences of the Moldavian SSR, Kishinev 277028. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1490-1492, November, 1983. Original article submitted May 17, 1983. All the sequential steps of this reaction have been studied in detail. Thus, the interconversions of isatins and o-aminophenylglyoxylic acids $(I \xrightarrow[H^+]{H^+} II)$ in alkaline and acid media

have long been known and often used in practice.

We have carried out a detailed study of the recyclization of α -(N-isatinyl) ketones to 2-acylindolyl-3-carboxylic acids (I \rightarrow II \rightarrow III) which is presently the only method for the preparation of these compounds.

The decarboxylation of previously isolated 2-acylindolyl-3-carboxylic acids (III \rightarrow IV) proceeds under the same conditions as for the direct synthesis of 2-acylindoles from N-phen-acylisatins and N-acetoylisatins. An example is given in the Experimental.

2-Acetonylindoles may be obtained in high yield if the synthesis is carried out in two steps with the prior isolation of 2-acetylindolyl-3-carboxylic acids [11, 13] and their subsequent decarboxylation in an organic base such as pyridine containing 0.04-0.05% alkali to accelerate the reaction [14]. We should note that 2-acylindolyl-3-carboxylic acids decarboxylate upon heating in both protic and aprotic solvents, in mixtures containing water and an organic base, and upon heating aqueous solutions of the alkali metal salts at reflux. In addition, the reaction may be accomplished thermally. In this case, 2-acetylindolyl-3-carboxylic acid is heated in an inert gas stream at 220-250°C. The 2-acylindoles formed are often colored by decomposition products but have a sharp melting point after purification.

Thus, 2-acylindoles are formed in weak alkaline or neutral mediawhich exclude the possibility of migration of the acyl group from $C_{(2)}$ or $C_{(3)}$.

The melting points, elemental analysis data, IR, UV, and mass spectra of the samples of 2-benzoyl- and 2-acetylindoles obtained in the present workwere identical to those reported by Sundberg [5] for these compounds obtained by a different method.

EXPERIMENTAL

The IR spectra were taken in vaseline oil on a UR-20 spectrometer. The syntheses of N-phenacylisatins [12, 16], N-acetonylisatins [13, 15, 16], and 2-aroylindolyl-3-carboxylic acids were reported in our previous work [11, 12].

<u>5-Bromo-2-benzoylindole</u>. A mixture of 49 ml DMF and 49 ml 10% aqueous NaOh was prepared and 2.41 g (7 mmoles) 5-bromo-N-phenacylisatin was added. The reaction mixture was heated at 60°C for 3 h and then cooled to 4°C. The precipitate (5-bromo-2-benzoylindole) was separated by filtration, washed with water until neutral, and dried in a dessicator over P_2O_5 to yield 1.92 g (91%) product with mp 215-216°C. IR spectrum: 3320 (NH), 1630 cm⁻¹ (C=O).

The other 2-aroylindoles were obtained by analogy (Table 1).

5-Methoxy-2-benzoylindole. A sample of 5-methoxy-2-benzoylindolyl-3-carboxylic acid (0.59 g) was heated in a nitrogen stream at 220-230°C for 10-12 min. The product formed, 5-methoxy-2-benzoylindole, was crystallized from 1:1 water-DMF and dried at 110°C for 2 h to yield 0.44 g (88%), mp 167-169°C.

Samples of 2-benzoylindole (86% yield) and 5-bromo-2-benzoylindole (70% yield) were prepared by analogy.

<u>2-Benzoylindole.</u> A. A mixture of 35 ml DMF and 35 ml water containing 3.5 g NaOH was prepared and 1.33 g 2-benzoylindolyl-3-carboxylic acid was added. The reaction mixture was heated for 210 min at 65°C and then cooled to 4°C. The precipitated product was filtered off, washed with water until neutral, and dried in a dessicator over P_2O_5 to yield 0.96 g (78%).

B. A solution of 0.53 g (2 mmoles) 2-benzoylindolyl-3-carboxylic acid in a mixture of 10 ml DMF and 3.1 ml water was prepared and 6.9 ml (0.002 mole) 0.29 M KOH was added. The reaction mixture was heated at reflux for 3 h and then cooled to 4°C. The precipitated product was washed with water and dried at 110°C for 2 h to give 0.4 g (91%), mp 149-150°C (151-152°C [5]). Samples of 2-(p-chlorobenzoyl)indole (88% yield), 5-bromo-2-benzoylindole (78% yield), and 2-(p-bromobenzoyl)indole (70% yield) were prepared by analogy.

<u>2-Acetylindolyl-3-carboxylic Acid.</u> A sample of 2 ml 20% aqueous NaOH was added to a solution of 1 g N-acetonylisatin in 100 ml water and stirred at 20°C for 70 min. The reaction mixture was then poured onto ice and acidified with 5% aq. sulfuric acid. The precipi-

TABLE 1. 2-Acylindoles

Ri	R²	R³	Mp, deg C	IR spectrum, cm ⁻¹		Yi - ld, %
				N—H	C=0	
$\begin{array}{c} C_{6}H_{5} \\ C_{6}H_{5} \\ C_{8}H_{5} \\ p\text{-}Br-\!\!-C_{6}H_{4} \\ p\text{-}Br-\!\!-C_{6}H_{4} \\ p\text{-}Cl-\!\!-C_{6}H_{4} \\ p\text{-}Cl-\!\!-C_{6}H_{4} \\ CH_{3} \end{array}$	H H CH₃ H H H H CH₃ H H H H	H CH ₃ O H Br CH ₃ H Br CH ₃ O	$\begin{array}{c} 149 -150 \\ 168 -169 \\ 171172 \\ 195196 \\ 234236 \\ 203204 \\ 236237 \\ 188189 \\ 133134 \\ 219220 \\ 206207 \\ 179180 \end{array}$	3315 3285 3310 3320 3315 3300 3320 3360 3300 3300 3300 3320	$\begin{array}{c} 1630 \\ 1620 \\ 1625 \\ 1630 \\ 1630 \\ 1660 \\ 1650 \\ 1665 \\ 1660 \\ 1660 \\ 1640 \end{array}$	77 72 73 88 80 78 78 97 80 92 85 89

tated product was filtered off, dried in the air, and then crystallized from ethanol to yield 0.9 g (90%), mp 217-218°C.

The other 2-acetylindolyl-3-carboxylic acids whose physical indices were given in our previous work [11, 13] were obtained by analogy.

<u>2-Acetylindole.</u> A. A sample of 0.035 ml 20% aq. NaOH was added to a suspension of 1.5 g 2-acetylindolyl-3-carboxylic acid in 15 ml pyridine and heated at reflux for 35 min. The homogeneous reaction mixture was cooled and 35 ml water was added. The precipitated product was filtered off and dried in a dessicator over P_2O_5 to yield 1.09 g (92%), mp 151.5-153°C (155°C [5]). The other 2-acetylindoles given in Table 1 were obtained by analogy.

B. A solution of 1 g 2-acetylindoly1-3-carboxylic acid in 50 ml ethyleneglycol was heated at reflux for 40 min, cooled, and then poured into 200 ml 5% aq. sodium bicarbonate. The precipitated product was filtered off, dried and recrystallized from benzene hexane to yield 0.47 g (60%).

C. A solution of 1 g 2-acetylindolyl-3-carboxylic acid was heated at reflux for 3 h in 15 ml DMF and then treated as in method B to yield 0.44 g (56%) product.

<u>5-Methyl-2-acetylindole.</u> A solution of 1.5 g 5-methyl-2-acetylindolyl-3-carboxylic acid in a mixture of 15 ml water and 3 ml triethylamine was prepared and heated at reflux for 210 min. The reaction solution was then diluted with 20 ml water and the precipitated product was filtered off, washed with water, dried, and crystallized from benzene hexane to yield 0.8 g (67%).

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INDO- AND BENZINDOCYANINE DYES WITH FLUORINE-CONTAINING SUBSTITUENTS

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Syntheses are reported for 2,3,3-trimethyl-3H-indoles and 1,1,2-trimethyl-1Hbenz[e]indoles with fluorine-containing substituents (CF_3 , CF_3S , and SO_2CF_3) at C-5 and for carbocyanine, merocyanine, and styryl dye derivatives of these indoles. The fluorine-containing substituents studied produce a bathochromic effect in the styryl dyes, hypsochromic effect in the merocyanine dyes, and, as a rule, a hypsochromic effect in the carbocyanine dyes.

Indocyanine dyes with substituents containing fluorine have been the subject of only a few studies. The effect of a trifluoromethyl group has been studied only at C-4, C-5, and C-6 in the case of indocarbocyanines [1]. Indolenines containing SCF_3 and SO_2CF_3 have been noted in the patent literature [2] but the syntheses for these compounds and the spectral characteristics of their dye derivatives were not given. Benzindolenines with fluorine-containing substituents have not been reported. We have obtained indolinines containing either a trifluoromethyl or trifluoromethylsulfonyl group at C-5 and benz[e]indolenines with a CF₃, SCF_3 , or SO_2CF_3 substituent at C-5. The spectral properties of carbocyanines, merocyanines and styryl dyes derived from these bases were studied.

Diazotization of p-trifluoromethylthioaniline [3] and reduction of the diazo salt by SnCl₂ gave p-trifluoromethylthiophenylhydrazine (I), which was then converted to the corresponding hydrazone. Fischer cyclization of this hydrazone gave indolenine II.



The yield of p-trifluoromethylsulfonylphenylhydrazine (III) by this method was low, the results had poor reproducibility, and the product was obtained in a mixture with the starting amine. The synthesis of hydrazine III was accomplished in 90% yield by the action of anhydrous hydrazine on p-trifluoromethylsulfonylchlorobenzene [4]. Hydrazine II was obtained previously by this same method, but in lower yield [5]. 2,3,3-Trifluoromethyl-5-trifluoromethylsulfonyl-3H-indole (IV) was prepared analogously to indolenine II.

The synthesis of 5-trifluoromethyl-, 5-trifluoromethylthio-, and 5-trifluoromethylsulfonyl derivatives of benzindolenines requires the development of methods of preparation for 3-nitronaphthalenes with these substituents at C-1. The fluorination of 3-nitro-1-naphthalenecarboxylic acid (V) [6] by highly pure sulfur tetrafluoride not containing HF leads to 1-trifluoromethyl-3-nitronaphthalene (VI) [7] in 40% yield. For this purpose, we used technical sulfur tetrafluoride without purification using a newly reported method for SF₄ fluorination in HF solution [8]. In the case of naphthalene derivatives, this method has limitations since HF is a catalyst for Friedel-Crafts reactions [9] and its presence may lead to the complete conversion of the reaction mixture into tars [7]. Acid V was fluorinated using SF₄ to tri-

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