CYANINE DYES FROM 2-METHYL-4,5,6,7-TETRAFLUOROBENZIMIDAZOLE DERIVATIVES

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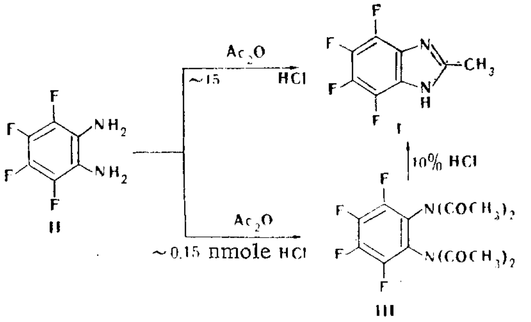
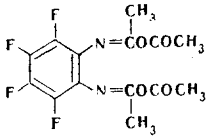
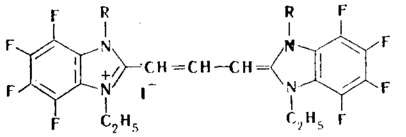
1-Ethyl-2-methyl-4,5,6,7-tetrafluorobenzimidazole was synthesized, and symmetrical and unsymmetrical imidacarbocyanines and merocyanines that are derivatives of N-ethylrhodanine were synthesized from it. It was established that complete replacement of the hydrogen atoms in the benzene ring of benzimidazole by fluorine leads to a decrease in the basicity of the imidacarbocyanine and a hypsochromic shift of the absorption maximum in series of imidacarbo- and imidadimethylidyne-merocyanines.

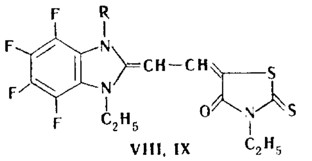
The introduction of halogen atoms in the benzene ring of benzimidazole leads to an increase in the sensitizing ability of tetraethylimidacarbocyanine [1]. Imidacarbocyanines that contain from one to four chlorine or bromine atoms in the benzene ring have been proposed as sensitizers for photographic emulsions [2-6]. We have previously obtained imidacyanine dyes that contain 5-fluoro- and 5,6-difluorobenzimidazole rings [7]. It seemed of interest to study the effect of complete replacement of the hydrogen atoms in the benzene ring of benzimidazole by fluorine atoms on the color and basicity of imidacyanine dyes.

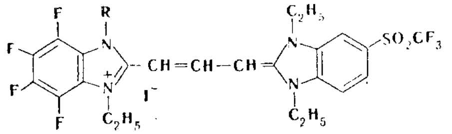
The 2-methyl-4,5,6,7-tetrafluorobenzimidazole (I) that is necessary for the synthesis of the dyes is obtained in high yield by the reaction of 3,4,5,6-tetrafluorophenylenediamine (II) [8] with acetic anhydride in both concentrated and dilute hydrochloric acid. However, we observed that refluxing II with acetic anhydride in the presence of catalytic amounts of hydrochloric acid leads to the formation of product III, which is also converted to benzimidazole I when it is heated in 10% hydrochloric acid.

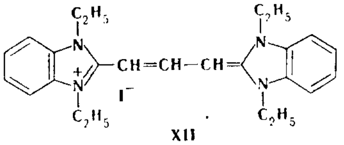



IV


VI, VII


VIII, IX


X, XI


XII

VI, VIII, X R = C_2H_5; VII, IX, XI R = $(CH_2)_2CF_3$

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TABLE 1. Fluoro-Substituted Imidacyanine Dyes (VI-XI)

Compound	mp,* °C (dec.)	F found, %	Empirical formula†	F calc., %	λ_{max} (*D*), nm		Yield, %
					alcohol	$CHCl_3$	
VI	215—217	22,8	$C_{25}H_{23}F_8IN_4$	23,1	492	504	16
VII	226—227	33,7	$C_{27}H_{21}F_{14}IN_4$	33,5	493	508	34
VIII	231—233	17,6	$C_{18}H_{17}F_4N_3OS_2$	17,6	510 (8)	510 (16)	40
IX	208—209‡	26,8	$C_{19}H_{16}F_7N_3OS_2$	26,6	509 (9,5)	506 (22)	37
X	233—234	18,1	$C_{26}H_{26}F_7IN_4O_2S$	18,5	508 (−1,5)	—	28
XI	234—235	—	$C_{27}H_{25}F_{10}IN_4O_2S$	—	508 (−1)	—	26

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*Dye VI was recrystallized from chlorobenzene, VII, X, and XI were recrystallized from alcohol, and VIII and IX were recrystallized from aqueous pyridine. †The compositions of dyes VI and VII were also confirmed by the results of a determination of the nitrogen content, while the compositions of dyes VII and XI were confirmed by the results of a determination of the carbon and hydrogen content. ‡Melts without decomposition.

We were unable to obtain a similar reaction product by the action of trifluoroacetic anhydride on diamine II. Only 2-trifluoromethyl-4,5,6,7-tetrafluorobenzimidazole is formed, regardless of the amount and concentration of hydrochloric acid [8]. It is possible that this is due to the easier hydrolysis of the tetrakis(trifluoroacetyl) derivative. Such unusual behavior of diamine II in solution in acetic anhydride made it necessary to rigorously prove the structure of III, since on the basis of the results of elementary analysis, it could be either the tetraacetyl derivative (III) or 3,4,5,6-tetrafluoro-N,N'-bis(1-acetoxyethylidene)phenylenediamine (IV). The possibility of the reaction of amines with acid anhydrides at the carbonyl group was previously demonstrated in the case of the reaction of 4,4'-diaminodiphenyl with phthalic anhydride [9]. The IR spectrum of III contains strong absorption bands at 1290 and 1700 cm^{-1}. The combination of these two bands is characteristic for an ester grouping [10]. At the same time, only one signal of protons of a CH_3 group is observed in the PMR spectrum. Data from the ^{13}C and ^{15}N NMR spectra constitute evidence in favor of tetraacetyl structure III. Five groups of signals with $^1J_{C-F}$ direct spin–spin coupling constants (SSCC) that are close to the constants obtained for compounds of the C_6F_5X series [11] are observed in the ^{13}C NMR spectrum. For structure IV one should have expected the presence of seven groups of signals, since the carbon atoms of the carbonyl and azomethine groups have different degrees of shielding. The ^{15}N chemical shift of tetraacetyl compound III (215.5 ppm) is substantially higher than that for a model compound of the IV type — perfluorobenzylideneaniline (56.9 ppm). At the same time, it is close to the chemical shift for trifluoroacetylperfluoroanilide (282.9 ppm). The absorption band at 1700 cm^{-1} in the IR spectrum of III is related to the vibrations of the C=O group, while the band at 1290 cm^{-1} is probably due to the vibrations of the polyfluoroaromatic ring.

The action of diethyl sulfate in an alkaline medium on benzimidazole I gave 1-ethyl-2-methyl-4,5,6,7-tetrafluorobenzimidazole (V). The latter by heating with ethyl or 3,3,3-trifluoropropyl p-toluenesulfonate was converted to the corresponding quaternary salts, from which symmetrical (VI, VII) and unsymmetrical (X, XI) carbocyanines, as well as merocyanines (VIII, IX), were synthesized (Table 1).

It is known that the introduction of substituents in the benzene ring of imidacarbocyanine dyes leads to deepening of their color. Small substituents with identical electronic natures in the 5 and 6 positions of the benzimidazole ring give rise to an approximately additive bathochromic shift of the absorption maximum; this is also valid for dyes that contain fluorine or chlorine atoms in the 5 and 6 positions. Complete replacement of the hydrogen atoms in the benzene ring of tetraethylimidacarbocyanine (XII) by chlorine leads to further deepening of its color [12]. In contrast to this, complete replacement of the hydrogen atoms by fluorine does not lead to a bathochromic shift but rather to a hypsochromic shift of the absorption maximum of tetraethylimidacarbocyanine (6 nm in the case of dye VI in alcohol). An appreciable hypsochromic shift of the absorption maximum of the dye is observed on passing from chloroform to a more polar solvent (alcohol) in the case of carbocyanines VI and VII, as well as imidacarbocyanines with electron-acceptor substituents in the benzene ring [13, 14].

When two, four, and eight chlorine atoms in the benzene ring of tetraethylimidacarbocyanine (XII), its basicity decreases gradually (pK_a 5.45, 4.98, 4.33, and 3.85 for dyes XII, 5,5'-Cl_2-XII, 5,5',6,6'-Cl_4-XII, and 4,4',5,5',6,6',7,7'-Cl_8-XII, respectively), whereas it increases in the case of two fluorine atoms in the 5 and 5' positions (pK_a 6.00). Similar influence of the electron-donor effect of conjugation of the fluorine atom is observed in the case of p-fluoroaniline, which is a slightly stronger base than aniline (pK_a 4.65 and 4.58, respectively [15]). The basicity of 5,5',6,6'-tetrafluoro-substituted dye XII (pK_a 5.45) is the same as that of unsubstituted carbocyanine XII. The electron-donor effect of conjugation of the fluorine atoms is evidently compensated by their electron-acceptor inductive effect. The introduction of another four fluorine atoms in the 4, 4', 7, and 7' positions leads to a decrease in the basicity (pK_a 4.28 for dye VI) owing to the fact that the electron-acceptor inductive effect of the fluorine atoms is manifested strongly in these positions.

In the case of imidadimethylidynemerocyanine (VIII) replacement of the hydrogen atoms by fluorine, as in the case of carbocyanine, leads to an increase in the color of the dye (in alcohol $\Delta\lambda_{max}$ 4 nm). A covalent structure predominates somewhat in alcohol and chloroform solutions of merocyanines (particularly IX), as evidenced by the tendency toward positive solvatochromism and a higher deviation (D) in chloroform solution. The deviations for unsymmetrical dyes X and XI are small, and this constitutes evidence for equalized electron density in the chromophores of these dyes.

EXPERIMENTAL

The UV spectra of solutions of the compounds in alcohol were recorded with a Specord UV-vis spectrophotometer. The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Varian A 56/60A spectrometer (60 MHz) with tetramethylsilane as the internal standard. The parameters of the ^{15}N and ^{13}C NMR spectra were obtained with a Bruker HX-90 pulse spectrometer at 9.12 and 22.63 MHz, respectively. The ^{15}N NMR spectra were for ^{15}N-enriched substances (95-96% ^{15}N). Solutions (20%) in CH_2Cl_2 were placed in a 10-mm ampul, into which a 5-mm ampul containing D_2O was inserted. The signal of the latter served as a control base for deuterium stabilization. A B-NC 12 laboratory computer was used for Fourier transformation and optimization of the spectra. The signal of $CH_3{}^{15}NO_2$ served as the external standard for recording the ^{15}N NMR spectra. The spectrometer conditions were as follows: The sweep width was 6024 Hz, the pulse width was 20 μsec (90°—pulse—30 μsec), and the time between pulses was 8 sec. The compounds used in the research were obtained by the methods in [16] from $(^{15}NH_4)_2SO_4$. The ^{13}C NMR spectrum was recorded without spin decoupling of the fluorine atoms. The chemical shift (δ in parts per million) is presented relative to tetramethylsilane (TMS) with CCl_4 (2-3%) as the relative standard, the chemical shift of which was taken as 96.0 ppm. The necessary signal/noise ratio was achieved by selection of the parameters: The pulse width was 10 μsec, the time lag between pulses was 10 sec, and the number of accumulations was 4500.

The basicities of the imidacarbocyanines (pK_a) were determined by the method in [17].

2-Methyl-4,5,6,7-tetrafluorobenzimidazole (I). A) A 2.87-g (16 mmole) sample of diamine II was refluxed with 22 ml (230 mmole) of acetic anhydride and 1 ml (12 mmole) of 36% hydrochloric acid for 14 h, after which 20 ml (240 mmole) of 36% hydrochloric acid was added, and the mixture was refluxed for another 4 h. The base was precipitated by the addition of ammonia until the mixture was weakly alkaline. The dried product was washed with benzene and sublimed *in vacuo* (2.67 Pa) at 150-160°C (bath temperature) to give 2.87 g (88%) of benzimidazole I with mp 248-249°C (from benzene with acetone or from alcohol with water). The product was quite soluble in alcohol, somewhat less soluble in acetone, slightly soluble in ether, virtually insoluble in chloroform, and soluble with difficulty in 20% HCl. ^{15}N NMR spectrum: 198.9 (s, —N=) and 356.9 ppm (s, —NH—) (a broad signal at 341 ppm is observed in the ^{15}N NMR spectrum of diamine II). Found: F 37.0%. $C_8H_4F_4N_2$. Calculated: F 37.2%.

B) A 0.5-g (1.44 mmole) sample of tetraacetyl compound III was refluxed in 10 ml (30 mmole) of 10% hydrochloric acid, and the precipitate was removed by filtration and dissolved in methanol. Ammonia gas was passed through the solution to give 0.12 g (40%) of benzimidazole I with mp 248-249°C, which was identical to the compound obtained by method A.

3,4,5,6-Tetrafluoro-N,N'-bis(diacetyl)-o-phenylenediamine (III). A mixture of 0.72 g (4 mmole) of diamine II, two drops (∿0.6 mmole) of 36% hydrochloric acid, and 3 ml (30 mmole) of acetic anhydride was refluxed for 3 h, after which it was poured into water. Workup gave 1.14 g (81%) of a product with mp 173-174°C (from petroleum ether with bp 70-100°C). UV spectrum (in alcohol), λ_{max} (log ε): 208 (4.18) and 268 nm (3.12). PMR spectrum (CCl_4): 2.2 ppm (s, CH_3). ^{13}C NMR spectrum (CH_2Cl_2): 172.1 (d, C=O), 145.0 (dd, 2-C, 5-C, $^1J_{C-F} = -251.9$ Hz), 142.0 (dt, 3-C, 4-C, $^1J_{C-F} = -264.3$ Hz), 123.8 (broad s, 1-C, 6-C), and 25.5 ppm (q, CH_3, $^1J_{C-H} = 130.5$ Hz). Found: C 48.2; H 3.5; F 21.7; N 8.3%; M 352. $C_{14}H_{12}F_4N_2O_4$. Calculated: C 48.3; H 3.5; F 21.8; N 8.0%; M 348.

1-Ethyl-2-methyl-4,5,6,7-tetrafluorobenzimidazole (V). A 1.5-ml (11 mmole) sample of diethyl sulfate was added to a heated (to 90-95°C) solution of 1.43 g (7 mmole) of benzimidazole I in 15 ml (40 mmole) of 10% sodium hydroxide, and the mixture was heated at 100°C for 30 min. It was then treated with 0.3 ml (2 mmole) of diethyl sulfate, and the mixture was heated for another 30 min and worked up to give 1.26 g (77.5%) of benzimidazole V with mp 100-101°C (from heptane). Found: F 32.6%. $C_{10}H_8F_4N_2$. Calculated: F 32.7%.

1-Ethyl-2-methyl-3-R-4,5,6,7-tetrafluorobenzimidazolium Toluenesulfonates. These compounds were obtained by heating 0.23 g (1 mmole) of benzimidazole V with 1.2 mmole of ethyl or 3,3,3-trifluoropropyl p-toluenesulfonate at 150°C for 5 h. 1,3-Diethyl-2-methyl-4,5,6,7-tetrafluorobenzimidazolium toluenesulfonate, with mp 189-190°C (after two precipitations from acetone by the addition of ether), was obtained in 96% yield. Found: C 52.8; H 4.7; F 17.7%. $C_{19}H_{20}F_4N_2O_3S$. Calculated: C 52.8; H 4.6; F 17.6%. 1-Ethyl-2-methyl-3,3,3-trifluoropropyl-4,5,6,7-tetrafluorobenzimidazolium toluenesulfonate, with mp 168-169°C (from acetone), was obtained in 75% yield. Found: F 26.8%. $C_{20}H_{19}F_7N_2O_3S$. Calculated: F 26.6%.

Carbocyanines VI and VII (Table 1). A mixture of 0.5 g (∿1 mmole) of the corresponding benzimidazolium toluenesulfonate, 1 ml (6 mmole) of ethyl orthoformate, and 5 ml of dimethylacetamide containing two drops [26.3 mg (∿0.5 mmole)] of acetic acid was heated with stirring without access to air moisture at 150°C for 3 h. For the isolation of dye VI, an aqueous solution of potassium iodide was added to the mixture, and the reaction product was extracted with chloroform and chromatographed on aluminum oxide (elution with nitrobenzene). Dye VII was precipitated from the reaction solution with a mixture (5:3) of hexane with ether and washed with hexane and water. It was then converted to the iodide by adding potassium iodide to an alcohol solution of the dye.

Imidadimethylidynemerocyanines VIII and IX (Table 1). Equimolar amounts (0.6 mmole of each) of the corresponding toluenesulfonate, 3-ethyl-5-acetanilidomethylenerhodanine, and triethylamine were refluxed in 7 ml of pyridine for 45 min. The dyes were precipitated with water and washed with water and alcohol.

Unsymmetrical Imidacarbocyanines X and XI (Table 1). A mixture of 0.55 mmole of the corresponding benzimidazolium toluenesulfonate, 0.55 mmole of 1,3-diethyl-2-(2-anilinovinyl)-5-trifluoromethylsulfonylbenzimidazolium iodide, 0.07 g (0.7 mmole) of acetic anhydride, 0.07 g (0.7 mmole) of triethylamine, and 3 ml of pyridine was refluxed for 7 min. The dyes were precipitated with heptane and washed with heptane and water. The dyes were converted to the iodides by adding potassium iodide to solutions in alcohol.

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SYNTHESIS OF FLUORINE-CONTAINING TETRASUBSTITUTED PYRIMIDINES FROM 1-CYANO-2-CHLORO-2-TRIFLUOROMETHYLETHYLENES

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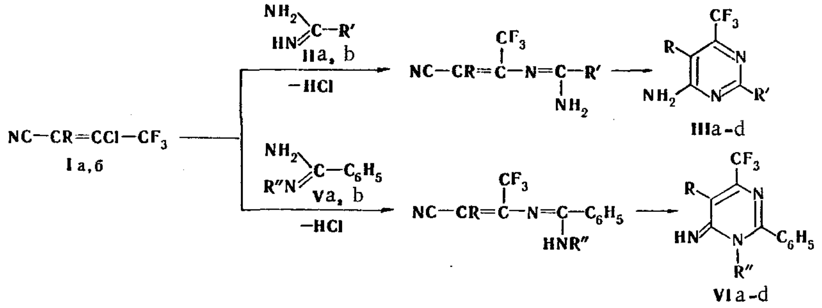
The condensation of 1,1-dicyano- and 1-trifluoromethylthio-1-cyano-2-chloro-2-trifluoromethylethylenes with amidines of trifluoro- or trichloroacetic acid gave 2,4-bis(trifluoromethyl)(or 2-trichloromethyl-4-trifluoromethyl)-5-cyano(or 5-trifluoromethylthio)-6-aminopyrimidines. The corresponding substituted 1-methyl(or 1-phenyl)-6(1H)-pyrimidineimines were synthesized by condensation of the same ethylenes with N-methyl(or N-phenyl)benzamidines.

We have previously shown that 2-trifluoromethyl-substituted 1-cyano-2-chloroethylenes, which are extremely reactive compounds, can be used for the synthesis of diverse heterocyclic compounds [1, 2]. In the present paper we describe a method for the preparation of fluorine-containing polyfunctional derivatives of pyrimidine. The method consists in the reaction of 2-trifluoromethyl-1-cyano-2-chloroethylenes (Ia, b) with acid amidines IIa, b. The initial products are evidently those formed by replacement of the chlorine atom in I, which subsequently undergo cyclization to 4-trifluoromethyl-6-aminopyrimidines (IIIa-d).



Ia, IIIa, b, VIa, b R=CN; Ib, IIIc,d, VIc,d R=SCF$_3$; IIa, IIIa, c, R'=CCl$_3$; IIb, IIIb,d R'=CF$_3$; Va, VIa, c R''=CH$_3$; Va, VIb,d R''=C$_6$H$_5$

We used this method to obtain pyrimidines that contain various substituents (see Table 1), which can be used to obtain a large number of other pyrimidine derivatives. From 1,1-dicyano-2-chloroethylene and trifluoroacetamidine by a similar method we synthesized 2-trifluoromethyl-5-cyano-4-aminopyrimidine (IV), which was previously obtained by condensation of the same trifluoroacetamidine with ethoxymethylenemalonodinitrile [3].

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