US 20110105754A1

(19) **United States**

(12) **Patent Application Publication**

**Filosa et al.**

(10) **Pub. No.: US 2011/0105754 A1**

(43) **Pub. Date: May 5, 2011**

(54) **NOVEL RHODAMINE DYES**

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(21) Appl. No.: **12/939,009**

(22) Filed: **Nov. 3, 2010**

**Related U.S. Application Data**

(63) Continuation of application No. 11/433,810, filed on May 12, 2006, now abandoned.

(60) Provisional application No. 60/680,088, filed on May 12, 2005, provisional application No. 60/680,212, filed on May 12, 2005.

**Publication Classification**

(51) **Int. Cl.**
***C07D 493/10*** (2006.01)

(52) **U.S. Cl.** ..... **546/15**; 549/227; 548/407

(57) **ABSTRACT**

There are described novel rhodamine color-forming compounds. The rhodamine color-forming compounds exhibit a first color when in a crystalline form and a second color, different from the first color, when in an amorphous form.

# NOVEL RHODAMINE DYES

## REFERENCE TO RELATED APPLICATIONS

**[0001]** This application claims the benefit of priority of provisional patent application Ser. Nos. 60/680,088 and 60/680,212, both filed May 12, 2005, the contents of which are incorporated herein by reference in their entireties.

**[0002]** This application is related to the following commonly assigned, United States patent applications and patents, the contents of which are incorporated herein by reference in their entireties:

**[0003]** U.S. Pat. No. 6,801,233 B2;

**[0004]** U.S. Pat. No. 6,906,735 B2;

**[0005]** U.S. Pat. No. 6,951,952 B2;

**[0006]** U.S. Pat. No. 7,008,759 B2;

**[0007]** U.S. patent application Ser. No. 10/806,749, filed Mar. 23, 2004, which is a division of U.S. Pat. No. 6,801,233 B2;

**[0008]** United States Patent Application Publication No. U52004/0176248 A1; (Attorney docket No. A-8544AFP);

**[0009]** United States Patent Application Publication No. US2004/0204317 A1; (Attorney Docket No. A-8586AFP);

**[0010]** United States Patent Application Publication No. US2004/0171817 A1; (Attorney Docket No. A-8589AFP);

**[0011]** U.S. patent application Ser. No. (11/400,735; filed on Apr. 6, 2006 (Attorney Docket No. A-8598);

**[0012]** U.S. patent application Ser. No. (11/400,734; filed on Apr. 6, 2006 (Attorney Docket No. A-8606); and

**[0013]** U.S. patent application Ser. No. (_____ filed on even date herewith, Express Mail No.: EV 669114278 US (Attorney Docket No. A-8608).

## FIELD OF THE INVENTION

**[0014]** This invention relates to novel rhodamine color-forming materials and, more particularly, to such color-forming materials that exhibit one color in a crystalline form and a second, different color in an amorphous form.

## BACKGROUND OF THE INVENTION

**[0015]** The development of thermal print heads (linear arrays of individually-addressable heating elements) has led to the development of a wide variety of thermally-sensitive imaging materials. In some of these, known as "thermal transfer" systems, heat is used to move colored material from a donor sheet to a receiver sheet. Alternatively, heat may be used to convert a colorless coating on a single sheet into a colored image, in a process known as "direct thermal" imaging. Direct thermal imaging has the advantage over thermal transfer of the simplicity of a single sheet. On the other hand, unless a fixing step is incorporated, direct thermal systems are still sensitive to heat after thermal printing. If a stable image is needed from an unfixed direct thermal system, the temperature for coloration must be higher than any temperature that the image is likely to encounter during normal use. A problem arises in that the higher the temperature for coloration, the less sensitive the imaging member will be when printed with the thermal print head. High sensitivity is important for maximum speed of printing, for maximizing the longevity of the print head, and for energy conservation in mobile, battery-powered printers. As described in more detail below, maximizing sensitivity while maintaining stability is more easily achieved if the temperature of coloration of a direct thermal medium is substantially independent of the heating time.

**[0016]** Known in the art are direct thermal imaging systems wherein an image is formed directly in the imaging member and thermal transfer thermal imaging systems wherein image-forming material is transferred, by the application of thermal energy, from a donor member to an image-receiving member. Various mechanisms to achieve image formation have been described in the thermal imaging art.

**[0017]** U.S. patent application Ser. No. 10/789,648, filed Feb. 27, 2004 (United States Patent Application Publication No. US2004/0176248 A1; Attorney Docket No. A-8544AFP), and assigned to the same assignee as the present application, is directed to a thermal imaging method wherein a dye is converted from one form in which the dye has one color to another form in which the dye has a second color, e.g., from colorless to colored.

**[0018]** Japanese Patent No. JP1997241553 discloses an ink jet recording liquid which includes asymmetrical rhodamine dyes. U.S. Pat. No. 4,390,616 discloses thermal imaging members and methods utilizing certain rhodamine dyes.

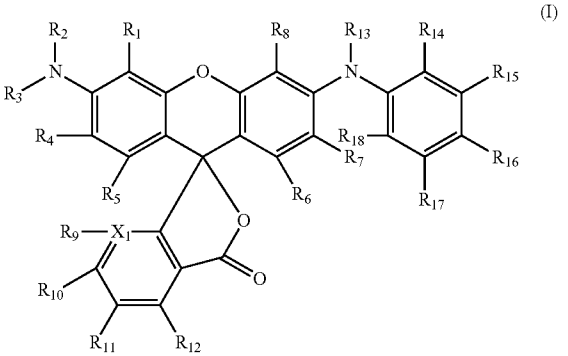
**[0019]** As the state of the imaging art advances and efforts are made to provide new imaging systems that can meet new performance requirements, and to reduce or eliminate some of the undesirable characteristics of the known systems, it would be advantageous to have new dyes which are suitable for use in imaging systems as well as in other applications.

## SUMMARY OF THE INVENTION

**[0020]** It is therefore an object of this invention to provide novel rhodamine dyes.

**[0021]** Another object of the invention is to provide such dyes that exhibit different colors when in the crystalline form and in the amorphous liquid form.

**[0022]** According to one aspect of the invention there are provided novel rhodamine dye compounds that exhibit a first color when in a crystalline form and a second color, different from the first color, when in an amorphous form, and which are represented by formula I




**[0023]** wherein:

**[0024]** $R_1$, $R_3$, $R_4$, $R_5$, $R_6$, $R_7$, $R_8$ and $R_{14}$ are each independently selected from the group consisting of hydrogen, substituted or unsubstituted alkyl, preferably having from 1 to 18 carbon atoms, alkenyl or substituted alkenyl, preferably having from 1 to 18 carbon atoms, heterocycloalkyl, substituted heterocycloalkyl alkoxy, substituted alkoxy, substituted carbonyl, acylamino and halogen;

**[0025]** $R_2$ is selected from the group consisting of hydrogen, alkyl and substituted alkyl, preferably having from 1 to

18 carbon atoms, alkenyl and substituted alkenyl, preferably having from 1 to 18 carbon atoms, heterocycloalkyl and substituted heterocycloalkyl; or

**[0026]** $R_2$ and $R_3$ taken together with the nitrogen atom to which they are attached can form a substituted or unsubstituted saturated heterocyclic ring system, such as, for example, substituted and unsubstituted morpholines, pyrrolidines, and piperidines;

**[0027]** $R_9$ is absent or selected from the group consisting of hydrogen, substituted or unsubstituted alkyl, preferably having from 1 to 18 carbon atoms, substituted or unsubstituted alkenyl, preferably having from 1 to 18 carbon atoms, heterocycloalkyl, substituted heterocycloalkyl, alkoxy, substituted alkoxy, substituted carbonyl, halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, amino, substituted amino, alkylamino, substituted alkylamino, arylamino and substituted arylamino;

**[0028]** $R_{10}$, $R_{11}$ and $R_{12}$ are each independently selected from the group consisting of hydrogen, substituted or unsubstituted alkyl, preferably having from 1 to 18 carbon atoms, substituted or unsubstituted alkenyl, preferably having from 1 to 18 carbon atoms, heterocycloalkyl, substituted heterocycloalkyl, alkoxy, substituted alkoxy, substituted carbonyl, halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, amino, substituted amino, alkylamino, substituted alkylamino, arylamino and substituted arylamino;

**[0029]** $R_{13}$ is selected from the group consisting of hydrogen, substituted or unsubstituted alkyl, preferably having from 1 to 18 carbon atoms, substituted or unsubstituted alkenyl, preferably having from 1 to 18 carbon atoms, heterocycloalkyl and substituted heterocycloalkyl;

**[0030]** $R_{14}$ is selected from the group consisting of hydrogen, substituted or unsubstituted alkyl, preferably having from 1 to 18 carbon atoms, substituted or unsubstituted alkenyl, preferably having from 1 to 18 carbon atoms, heterocycloalkyl and substituted heterocycloalkyl; or

**[0031]** $R_{13}$ and $R_{14}$ taken together with the atoms to which they are attached can form a 5- or 6-membered heterocyclic ring such as, for example, indoline or tetrahydroquinoline;

**[0032]** $R_{15}$, $R_{16}$, $R_{17}$ and $R_{18}$ are each independently selected from the group consisting of hydrogen, substituted or unsubstituted alkyl, preferably having from 1 to 18 carbon atoms, substituted or unsubstituted alkenyl, preferably having from 1 to 18 carbon atoms, heterocycloalkyl, substituted heterocycloalkyl, alkoxy, substituted alkoxy, substituted carbonyl, halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, amino, substituted amino, alkylamino, substituted alkylamino, arylamino and substituted arylamino; and

**[0033]** $X_1$ is carbon or nitrogen;

**[0034]** and only one of $R_2$ and $R_{13}$ is hydrogen.

**[0035]** The substituents are preferably chosen to minimize the water solubility of the compounds and facilitate the formation of a colorless form in non-polar, non-protic solvents. In turn, the colorless lactone form of the compounds must be capable of melting to form the colored form.

**[0036]** A preferred group of compounds according to the invention are those represented by formula I wherein $R_2$ and $R_3$ taken together form a pyrrolidine ring, $R_{10}$, $R_{11}$ and $R_{13}$ each is hydrogen, $X_1$ is carbon and $R_1$, $R_4$, $R_5$, $R_6$, $R_7$, $R_8$, $R_9$, $R_{12}$, $R_{14}$ and $R_{15}$-$R_{18}$ are as described with respect to formula I.

**[0037]** A second preferred group of compounds according to the invention are those represented by formula I wherein $R_2$ is hydrogen, $R_3$ is alkyl, $R_{10}$ and $R_{11}$ are each halogen, $R_{13}$ is alkyl, $X_1$ is carbon and $R_1$, $R_4$, $R_5$, $R_6$, $R_7$, $R_8$, $R_9$, $R_{12}$, $R_{14}$ and $R_{15}$-$R_{18}$ are as described with respect to formula I.

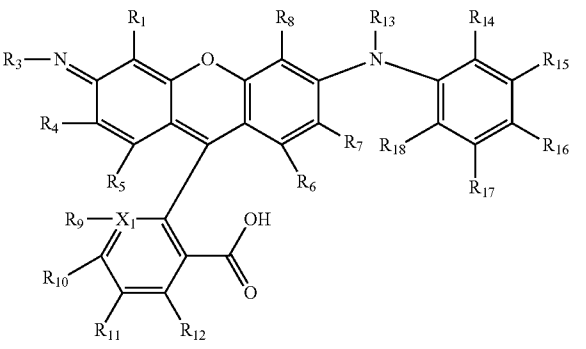
**[0038]** Particularly preferred rhodamine compounds according to the invention are those represented by formula I in which $R_1$, $R_4$, $R_5$, $R_6$, $R_7$, $R_8$, $R_9$ and $R_{12}$ are each hydrogen; $R_2$ is hydrogen or alkyl having from 1-18 carbon atoms, $R_3$ is alkyl having from 1-18 carbon atoms, or $R_2$ and $R_3$ taken together with the nitrogen atom to which they are attached form a pyrrolidine ring; $R_{10}$ and $R_{11}$ are each independently hydrogen or halogen; $R_{13}$ is hydrogen or alkyl, preferably having from 1-18 carbon atoms, $R_{14}$ is hydrogen or alkyl having from 1-18 carbon atoms, $X_1$ is carbon and $R_{15}$-$R_{18}$ are each independently hydrogen, alkyl having from 1-18 carbon atoms, or halogen.

**[0039]** The conversion from the crystalline form to the liquid form, such as in accordance with the use of the compounds in thermal imaging members and thermal imaging methods, is carried out by applying heat to the compounds. In thermal imaging methods, thermal energy may be applied to the thermal imaging members by any of the techniques known in thermal imaging such as from a thermal print head, a laser, a heated stylus, etc.

**[0040]** The novel dyes of the invention are useful in a variety of applications including thermal imaging members and thermal imaging methods. Particularly preferred thermal imaging members and thermal imaging methods, which utilize unsymmetrical rhodamine compounds, including the novel compounds of the present invention, are disclosed and claimed in co-pending commonly assigned U.S. patent application Ser. No. _____, Express Mail No.: EV 669114278 US (Attorney Docket No. A-8608).

**[0041]** When converted to the colored form the compounds of formula I have the open form illustrated by formula II (for the case where $R_2$ in formula I is hydrogen)

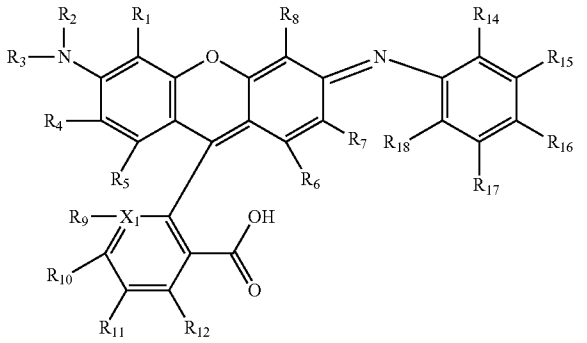
(II)




**[0042]** wherein R1, and R3-R18 are as defined above with respect to formula I,

**[0043]** or formula III (for the case where $R_{13}$ in formula I is hydrogen)

(III)



**[0044]** wherein $R_1$-$R_{12}$ and $R_{14}$-$R_{18}$ are as defined above with respect to formula I.

## DETAILED DESCRIPTION OF THE INVENTION

**[0045]** Compounds in the crystalline state commonly have properties, including color, that are very different from those of the same compounds in an amorphous form. In a crystal, a molecule is typically held in a single conformation (or, more rarely, in a small number of conformations) by the packing forces of the lattice. Likewise, if a molecule can exist in more than one interconverting isomeric forms, only one of such isomeric forms is commonly present in the crystalline state. In amorphous form or solution, on the other hand, the compound may explore its whole conformational and isomeric space, and only a small proportion of the population of individual molecules of the compound may at any one time exhibit the particular conformation or isomeric form adopted in the crystal. Compounds of the present invention exhibit tautomerism in which at least one tautomeric form is colorless, and at least another tautomeric form is colored. The crystalline form of compounds of the present invention comprises predominantly the colorless tautomer.

**[0046]** Specific representative compounds according to the invention are those of formula I which are shown in Table I in which the substituents $R_1$, $R_4$, $R_5$, $R_6$, $R_7$, $R_8$, $R_9$, $R_{11}$ and $R_{15}$-$R_{18}$ are all hydrogen, $X_1$ is carbon and $R_2$, $R_3$, $R_{10}$, $R_{11}$, $R_{13}$ and $R_{14}$ are as shown:

TABLE I

| DYE | $R_2$ | $R_3$ | $R_{10}$ | $R_{11}$ | $R_{13}$ | $R_{14}$ | (X2)n | M.P. | λmax |
|---|---|---|---|---|---|---|---|---|---|
| I | n-C10H21 | H | H | H | —$(CH_2)_3$— | | H | 124 | 570 |
| II | Cyclohexyl | H | H | H | C2H5 | H | H | 212 | 544 |
| III | Adamantyl | H | H | H | C2H5 | H | H | 240 | 544 |
| IV | Cyclohexyl | H | Cl | Cl | C4H9 | H | H | 193 | 554 |
| V | Adamantyl | H | Cl | Cl | C4H9 | H | H | 252 | 554 |
| VI | Cyclohexyl | H | Cl | Cl | C8H17 | H | H | 162 | 554 |
| VII | —$(CH_2)_4$— | | H | H | H | CH3 | H | 268 | 556 |
| VIII | —$(CH_2)_4$— | | H | H | H | CH3 | 4-F | 272 | 552 |
| IX | —$(CH_2)_3CHCH_3$— | | H | H | H | CH3 | 4-F | 228 | 552 |

## DEFINITIONS

**[0047]** The term "alkyl" as used herein refers to saturated straight-chain, branched-chain or cyclic hydrocarbon radicals. Examples of alkyl radicals include, but are not limited to, methyl, ethyl, propyl, isopropyl, n-butyl, tert-butyl, neopentyl, n-hexyl, cyclohexyl, n-octyl, n-decyl, n-dodecyl and n-hexadecyl radicals.

**[0048]** The term "alkenyl" as used herein refers to unsaturated straight-chain, branched-chain or cyclic hydrocarbon radicals. Examples of alkenyl radicals include, but are not limited to, allyl, butenyl, hexenyl and cyclohexenyl radicals.

**[0049]** The term "alkynyl" as used herein refers to unsaturated hydrocarbon radicals having at least one carbon-carbon triple bond. Representative alkynyl groups include, but are not limited to, ethynyl, 1-propynyl, 1-butynyl, isopentynyl, 1,3-hexadiynyl, n-hexynyl, 3-pentynyl, 1-hexen-3-ynyl and the like.

**[0050]** The terms "halo" and "halogen," as used herein, refer to an atom selected from fluorine, chlorine, bromine and iodine.

**[0051]** The term "aryl," as used herein, refers to a mono-, bicyclic or tricyclic carbocyclic ring system having one, two or three aromatic rings including, but not limited to, phenyl, naphthyl, anthryl, azulyl, tetrahydronaphthyl, indanyl, indenyl and the like.

**[0052]** The term "heteroaryl," as used herein, refers to a cyclic aromatic radical having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon, the radical being joined to the rest of the molecule via any of the ring atoms, such as, for example, pyridinyl, pyrazinyl, pyrimidinyl, pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, isooxazolyl, thiadiazolyl, oxadiazolyl, thiophenyl, furanyl, quinolinyl, isoquinolinyl, and the like.

**[0053]** The term "heterocycloalkyl," as used herein, refers to a non-aromatic 3-, 4-, 5-, 6- or 7-membered ring or a bi- or tri-cyclic group comprising fused six-membered rings having between one and three heteroatoms independently selected from oxygen, sulfur and nitrogen, wherein (i) each 5-membered ring has 0 to 1 double bonds and each 6-membered ring has 0 to 2 double bonds, (ii) the nitrogen and sulfur heteroatoms may optionally be oxidized, (iii) the nitrogen heteroatom may optionally be quaternized, and (iv) any of the above heterocyclic rings may be fused to a benzene ring. Representative heterocycles include, but are not limited to, pyrrolidinyl, pyrazolinyl, pyrazolidinyl, imidazolinyl, imidazolidinyl, piperidinyl, piperazinyl, oxazolidinyl, isoxazolidinyl, morpholinyl, thiazolidinyl, isothiazolidinyl, and tetrahydrofuryl.

**[0054]** The term "carbonyl" as used herein refers to a carbonyl group, attached to the parent molecular moiety through the carbon atom, this carbon atom also bearing a hydrogen

atom, or in the case of a "substituted carbonyl" a substituent as described in the definition of "substituted" below.

**[0055]** The term "acyl" as used herein refers to groups containing a carbonyl moiety. Examples of acyl radicals include, but are not limited to, formyl, acetyl, propionyl, benzoyl and naphthoyl.

**[0056]** The term "alkoxy", as used herein, refers to a substituted or unsubstituted alkyl, alkenyl or heterocycloalkyl group, as previously defined, attached to the parent molecular moiety through an oxygen atom. Examples of alkoxy radicals include, but are not limited to, methoxy, ethoxy, propoxy, isopropoxy, n-butoxy, tert-butoxy, neopentoxy and n-hexoxy.

**[0057]** The term "aryloxy" as used herein refers to a substituted or unsubstituted aryl or heteroaryl group, as previously defined, attached to the parent molecular moiety through an oxygen atom. Examples of aryloxy include, but are not limited to, phenoxy, p-methylphenoxy, naphthoxy and the like.

**[0058]** The term "alkylamino", as used herein, refers to a substituted or unsubstituted alkyl, alkenyl or heterocycloalkyl group, as previously defined, attached to the parent molecular moiety through a nitrogen atom. Examples of alkylamino radicals include, but are not limited to, methylamino, ethylamino, hexylamino and dodecylamino.

**[0059]** The term "arylamino", as used herein, refers to a substituted or unsubstituted aryl or heteroaryl group, as previously defined, attached to the parent molecular moiety through a nitrogen atom.

**[0060]** The term "substituted" as used herein in phrases such as "substituted alkyl", "substituted alkenyl", "substituted aryl", "substituted heteroaryl", "substituted heterocycloalkyl", "substituted carbonyl", "substituted alkoxy", "substituted acyl", "substituted amino", "substituted aryloxy", and the like, refers to independent replacement of one or more of the hydrogen atoms on the substituted moiety with substituents independently selected from, but not limited to, alkyl, alkenyl, heterocycloalkyl, alkoxy, aryloxy, hydroxy, amino, alkylamino, arylamino, cyano, halo, mercapto, nitro, carbonyl, acyl, aryl and heteroaryl groups.

**[0061]** The term "substituted" as used herein in phrases such as "substituted nitrogen", "substituted oxygen" and "substituted sulfur" refers to nitrogen, oxygen or sulfur substituted with alkyl, aryl, or heteroaryl groups. Examples include, but are not limited to, alkyl and aryl ethers such as methoxy, ethoxy or phenoxy; alkyl or aryl thioethers such as thiomethoxy, thioethoxy and thiophenyl; alkyl or aryl amines such as dimethyl amino, diethylamino, diphenylamino, phenylamino, and N-methyl-N-phenylamino.

**[0062]** According to the invention, there are provided molecules exhibiting tautomerism in which at least one tautomeric form is colorless, and at least another tautomeric form is colored. Crystallization of the equilibrating mixture of the two tautomeric forms is carried out so as to produce colorless crystals. The solvent chosen to perform the crystallization will typically be one of such polarity (and other chemical properties, such as hydrogen-bonding ability) that the pure colorless crystal form is favored, either in the equilibrium between the colorless and colored forms in solution, or in having lower solubility in the solvent than the colored form. The choice of solvent is usually determined empirically for a particular mixture of tautomers.

**[0063]** Upon conversion of the pure crystalline colorless form to an amorphous form, the equilibrium between the two tautomers is re-established. The proportion of the amorphous material that is colored (i.e., the proportion that is in the colored tautomeric form) may vary, but is preferably at least about 10%.

**[0064]** The colored and colorless tautomeric forms of the molecules according to the present invention must meet certain criteria for image quality and permanence when used in thermal and other imaging applications. The colorless form, which is preferably the crystalline form, should have minimal visible absorption. It should be stable to light, heating below the melting point, humidity, and other environmental factors such as ozone, oxygen, nitrogen oxides, fingerprint oils, etc. These environmental factors are well known to those skilled in the imaging art. The colored, amorphous form should be stable also to the above mentioned conditions, and in addition should not recrystallize to the colorless form under normal handling conditions of the image. The colored form should have a spectral absorption appropriate for digital color rendition. Typically, the colored form should be yellow (blue-absorbing), magenta (green-absorbing), cyan (red absorbing), or black, without undue absorption in an unintended spectral region. For non-photographic applications, however, it may be required that the colored form not be one of the subtractive primary colors, but rather a particular spot color (for example, orange, blue, etc.).

**[0065]** The compounds according to the invention may be prepared by synthetic processes which are known to those skilled in the art, particularly in view of the state of the art and the specific preparatory examples provided below herein.

**[0066]** Generally, symmetrical rhodamine dyes can be prepared in one step from 3',6'-dichlorofluorans by reacting two equivalents of an aromatic or aliphatic amine as described in U.S. Pat. No. 4,602,263, GB2311075 and DE81056. The unsymmetrical rhodamine dyes are then prepared by the selective monoalkylation of, symmetrical rhodamines using sodium hydride in dimethyl sulfoxide as described in U.S. Pat. Nos. 4,602,263 and 4,826,976.

**[0067]** Alternatively these novel unsymmetrical rhodamines can be prepared by use of an alternate synthetic pathway in which one equivalent of an N-alkylaniline is reacted selectively with the 3',6'-dichlorofluoran using aluminum chloride as a catalyst to produce 3'-chloro-6'-N-alkyl-N-arylfluorans. These products are isolated and purified prior to reacting with a second equivalent of an aromatic or aliphatic amine. Zinc chloride is used as the catalyst for the second addition. DE139727 describes the selective addition of anilines to 3',6'-dichlorofluorans to produce 3'-chloro-6'-arylaminofluorans using a mixture of zinc chloride and zinc oxide at 160° C.

**[0068]** Unsymmetrical rhodamines can also be made from 2-benzoyl benzoic acid derivatives by condensation with 3-arylamino phenols or 3-alkylamino phenols as described in *Chemistry and Applications of Leuco Dyes*, pp. 180-191 R. Muthyala, Ed., Plenum Press, New York and London, 1997 and also U.S. Pat. Nos. 4,390,616 and 4,436,920.

**[0069]** To optimize the chromophore, melting point, degree of coloration, light stability and solubility of the dyes of this application a variety of anilines, N-alkylanilines, aliphatic amines and dichlorofluorans are utilized.

**[0070]** The 3',6'-dichlorofluorans are synthesized from the corresponding fluoresceins using thionyl chloride and dimethylformamide in a variation of the method of Hurd described in the Journal of the Amer. Chemical Soc. 59, 112 (1937).

**[0071]** Careful recrystallization from solvent mixtures such as hexanes/acetone or hexanes/ethyl acetate produces white crystalline material that is preferred for use in thermal imaging members.

## EXAMPLES

**[0072]** The invention will now be described further in detail with respect to specific embodiments by way of examples, it being understood that these are intended to be illustrative only and the invention is not limited to the materials, amounts, procedures and process parameters, etc. recited therein. All parts and percentages recited are by weight unless otherwise specified.

### Example I

#### Synthesis of N-acetyl-N-octylaniline

**[0073]** 1-Octyl bromide (39 mL, 224 mmol, 1.12 eq) was added dropwise to a mixture of acetanilide (27 g, 200 mmol, 1 eq.) in dimethylsulfoxide (130 mL), containing potassium hydroxide pellets (18.87 g, 300 mmol, 1.5 eq.), at room temperature. After all the 1-octyl bromide was added the reaction mixture was heated to 50-55° C. for 1.5 hours. The reaction mixture was cooled and poured into water (1 L), stirred for 45 minutes and extracted with hexanes (3×400 mL). The hexane extracts were combined, dried over sodium sulfate and evaporated to give 48.4 g (196 mmol, 98%) of colorless oil. The product was identified by NMR spectroscopy and mass spectrometry and was used without further purification.

#### Synthesis of N-octylaniline

**[0074]** To N-acetyl-N-octylaniline (48.4 g, 196 mmol) was added 4N hydrochloric acid (100 mL) and the mixture heated to 100-110° C. and stirred at this temperature for 4 days. The reaction mixture was cooled to ambient temperature, diluted with water (100 mL), and hexanes (200 mL). The pH of the reaction mixture was brought to pH 14 by addition of 45% potassium hydroxide with cooling by an ice bath. The layers were separated and the aqueous layer washed with hexanes (100 mL). The combined organic layers were dried over sodium sulfate and concentrated by rotary evaporation to give the desired product as a light brown oil (40 g, 195 mmol, 99%). The product was identified by NMR spectroscopy and mass spectrometry and in general was used without further purification. Analytically pure product was obtained by distillation at reduced pressure: b.p. 145-150° C. (0.5 mm).

#### Synthesis of 5,6-dichlorofluorescein

**[0075]** To a 5 L 3-neck flask fitted with a mechanical stirrer and a thermometer was added 4,5-dichlorophthalic acid (502 g, 2.13 mol) and methanesulfonic acid (2 L). The mixture was stirred at 90° C. for one hour. The mixture was cooled to 80° C. and resorcinol (470 g, 4.27 mol) was added all at once. The dark mixture was heated at 105° C. for one hour. The warm mixture was poured into a stirred mixture of ice (6 kg) and water (5 L). The mixture was stirred for 30 minutes and filtered. The filter cake was washed with water (3×500 mL). The wet filter cake was stirred with propyl acetate (2 L) and filtered again. The wet cake was dried to a constant weight and placed in the original reaction vessel. Propyl acetate (2 L) was added and the stirred mixture was heated to 90° C. and allowed to cool to room temperature and filtered. The filter cake was washed with acetone (0.4 L) and hexane (0.4 L). The mustard yellow solid was dried to a constant weight in the vacuum oven to afford 930 g (109% yield).

#### Synthesis of 3',6',5,6-tetrachlorofluoran

**[0076]** To a 5 L 3-necked fitted with a mechanical stirrer, a thermometer, and a dropping funnel was added dichlorofluorescein (930 g, ca. 2.13 mol), sulfolane (2.4 L), and dimethylformamide (152 mL, 1.9 moles). The stirred mixture was warmed to 90° C. and phosphorus oxychloride (0.72 L) was added dropwise over one hour while keeping the temperature between 90 and 95° C. After the addition was complete, the mixture was kept at the same temperature for one hour and poured into acetone:water (2:1, 11 L). The mixture was stirred for one hour and filtered. The filter cake was washed with acetone: water (2 L) and dried in a vacuum oven to a constant weight. A beige solid was obtained. (805 g, 1.84 mol, 86% overall yield for two steps).

#### Synthesis of 3'-chloro-6'-tetrahydroquinolinofluoran

**[0077]** A mixture of dichlorofluoran (3.7 g, 0.01 mol), aluminum chloride (9 g, 0.07 mol) and tetrahydroquinoline (2.6 g, 0.02 moles) in sulfolane (25 ml) was held at 150° C. for 18 hours. The reaction mixture was quenched into 100 ml of water. The solid was filtered off, washed with water and dried. The product was purified on silica gel using 2% methanol in methylene chloride to yield 3'-chloro-6'-tetrahydroquinolinofluoran (250 mg, 0.54 mmol, 5.4%).

#### Synthesis of 3'-chloro-6'-(N-ethylaniline)-5,6-dichlorofluoran

**[0078]** A three-necked flask equipped with mechanic stirrer and thermometer was charged with 3',6',5,6-tetrachlorofluoran (8.8 g, 20 mmol) and 40 mL of sulfolane. Aluminum chloride (11.0 g, 80 mmol) was added to the mixture in portions with stirring. At 60° C., N-ethylaniline (6.05 g, 50 mmol, 2.5 eq.) was added dropwise over 15 minutes. The reaction was monitored by HPLC. After the starting materials were consumed, the reaction mixture was cooled and poured into 2 N HCl (500 mL). The precipitated solid was filtered, washed and air-dried. The free base was obtained by dissolving the salt in DMF, followed by pouring into ammonia hydroxide solution. The product was washed with water and dried. (Yield: 9.36 g, 17 mmol, 85%).

#### Synthesis of 3'-N-butylanilino-6'-chlorofluoran

**[0079]** 3',6'-Dichlorofluoran (15.0 g, 40.6 mmol) was taken up in sulfolane (80 mL), heated to 60° C. and aluminum chloride (21.0 g, 157.9 mmol, 3.9 eq.) was added in one portion. N-Butylaniline (15 mL, 98.3 mmol, 2.4 eq.) was then added dropwise over 5 minutes and the reaction was heated at 80° C. for 1 hour. The reaction mixture was poured into 3N hydrochloric acid and ice. The resulting precipitate was filtered, washed with water and dried overnight to afford the crude 3'-N-butylanilino-6'-chlorofluoran (18.9 g, 39.2 mmol, 96%) which was used as such.

#### Synthesis of 3'-chloro-6'-(N-octylaniline)-5,6-dichlorofluoran

**[0080]** To a solution of 3',6',5,6-tetrachlorofluorescein (8.8 g, 0.02 mol) in sulfolane (40 mL) was added aluminum chloride (11.0 g, 0.08 mol) in portions with stirring. This was followed by the addition of N-octylaniline (4.4 g, 0.022 mol)

at 50° C. over 5 minutes. After 30 minutes, triethylamine (6.0 g, 0.06 mol) was added dropwise over 10 minutes. After the starting materials were consumed (HPLC) the reaction mixture was cooled and poured into 2 N HCl (500 mL). The precipitated solid was filtered, washed and air-dried. The free base product was obtained by dissolving the salt in DMF, followed by pouring into ammonium hydroxide solution.

Synthesis of 3'-chloro-6'-(2-methylanilino)-fluoran

**[0081]** To a suspension of 3',6'-dichlorofluoran (30 g, 81 mmol) in sulfolane (120 mL) was added $AlCl_3$ (3.0 eq., 244 mmol, 32.4 g) and the mixture was warmed to 60° C. o-Toluidine (1.1 eq., 89.4 mmol 9.6 g) was added and the temperature of the orange solution was maintained at 60° C. for 10 minutes. Neat triethylamine (1.05 eq., 85.4 mmol, 8.64 g) was added dropwise with stirring over a period of 10 minutes. After stirring at 70° C. open to air for 4 hours, the solution was poured into a vigorously stirred beaker of water (1 L). The resulting suspension was filtered, and the collected solids were dissolved in ethyl acetate (500 mL). The organic extracts were dried over sodium sulfate and adsorbed on silica (~100 g). The product was purified by silica gel column chromatography (1:1 Hexane/ethyl acetate) to yield an orange solid. The product was identified by NMR spectroscopy and mass spectrometry.

Example II

Synthesis of Dye I

**[0082]** A mixture of 3'-chloro-6'-tetrahydroquinolinofluoran (100 mg, 0.2 mmol), decylamine (100 mg, 0.6 mmoles), and zinc chloride (100 mg, 0.7 mmol) in sulfolane (3 mL) was held at 150° C. for 3 hours. The reaction mixture was quenched into 10 ml of water. The solid was filtered off, washed with water and dried. The product was purified by silica gel chromatography using 2% methanol in methylene chloride to yield Dye I, 3'N-decylamino-6-tetrahydroquinoline fluoran as an off-white solid (42 mg, 0.07 mmol, 35%). The product was identified by NMR spectroscopy and mass spectrometry, m.p. 124° C.

Example III

Synthesis of Dye II

**[0083]** To a solution of 3'-N-ethylanilino-6'-chlorofluoran (1.82 g, 4 mmol) in 12 ml of sulfolane was added zinc chloride (1.63 g, 12 mmol), zinc oxide (0.32, 4 mmol) and cyclohexylamine (1.6 g, 16 mmol). The reaction mixture was heated to 140° C. under stirring overnight (18 hours). After being cooled to room temperature, the reaction mixture was poured into water (100 mL) and the precipitated crude product was obtained by filtration, dried in air and dissolved in methylene chloride (50 mL). After removing insoluble solids by filtration, the resulting filtrate was subjected to chromatography (silica gel, hexane/ethyl acetate as eluent). The isolated oil product was recrystallized in a mixed solution of hexane and ethyl acetate to give 0.7 g of Dye II as light pink crystals, m.p. 212-214° C. The product was identified by NMR spectroscopy and mass spectrometry.

Example IV

Synthesis of Dye III

**[0084]** To a solution of 3'-N-ethylanilino-6'-chlorofluoran (1.82 g, 4 mmol) in 12 ml of sulfolane was added zinc chloride (1.63 g, 12 mmol), zinc oxide (0.32, 4 mmol) and 1-adamantylamine (2.4 g, 16 mmol). The reaction mixture was heated to 150° C. under stirring overnight. After being cooled to room temperature, the reaction mixture was poured into 100 ml water, the precipitated crude product obtained by filtration and dried in vacuum and then dissolved in methylene chloride. After removal of insoluble solid, the resulting filtrate was concentrated to the appropriate volume for being loaded on chromatography (silica gel, hexane/ethyl acetate as eluent). The isolated oil, Dye III, crystallized as light pink crystals from a solution of hexane and ethyl acetate (0.55 g, m.p. 240-242° C.). The product was identified by NMR spectroscopy and mass spectrometry.

Example V

Synthesis of Dye IV

**[0085]** To a solution of 3'-chloro-6'-(N-butylanilino)-5,6-dichlorofluoran (2.2 g, 4 mmol) in 12 ml of sulfolane was added zinc chloride (1.63 g, 12 mmol), zinc oxide (0.32, 4 mmol) and cyclohexylamine 1.6 g, 16 mmol). The reaction mixture was heated to 140° C. under stirring overnight. After being cooled to room temperature, the reaction mixture was poured into water (100 mL) and the precipitated crude product was obtained by filtration, subjected to chromatography (silica gel, hexane/ethyl acetate as eluent) using methylene chloride as solvent for loading. The isolated oil product was recrystallized in hexane mixed with 30% of ethyl acetate to give Dye IV (0.56 g) as light pink crystals, m.p. 193-195° C. The product was identified by NMR spectroscopy and mass spectrometry.

Example VI

Synthesis of Dye V

**[0086]** To a solution of 3'-chloro-6'-(N-butylaniline)-5,6-dichlorofluoran (2.2 g, 4 mmol) in 12 ml of sulfolane was added zinc chloride (1.63 g, 12 mmol), zinc oxide (0.32, 4 mmol) and 1-adamantylamine (2.4 g, 16 mmol). The reaction mixture was heated to 150° C. under stirring overnight. After being cooled to room temperature, the reaction mixture was poured into water (100 mL) and the precipitated crude product obtained by filtration, dried in vacuum and directly subjected to chromatography (silica gel, hexane/ethyl acetate as eluent) with methylene chloride as loading solvent, ignoring insoluble solid. The isolated oil product was transformed into Dye V, as light pink crystals by recrystallization from a mixed solution of hexane and ethyl acetate (0.45 g, m.p. 252-254° C.). The product was identified by NMR spectroscopy and mass spectrometry.

Example VII

Synthesis of Dye VI

**[0087]** To a solution of 3'-chloro-6'-(N-octylaniline)-5,6-dichlorofluoran (1.82 g, 3 mmol) in 12 ml of sulfolane was added zinc chloride (1.30 g, 9 mmol), zinc oxide (0.25 g, 3 mmol) and cyclohexylamine (1.2 g, 12 mmol). The reaction mixture was heated to 140° C. under stirring overnight. After being cooled to room temperature, the reaction mixture was poured into 2 N HCl (100 mL), the precipitated crude product obtained by filtration, dried in vacuum and dissolved in DMF (20 mL). The mixed DMF solution was poured into 10% ammonium hydroxide (100 mL). The resulting red crude

product was subjected to chromatography (silica gel, hexane/ethyl acetate as eluent) for further purification. The isolated oil product was converted into Dye VI as light pink crystals by recrystallization from a mixed solution of hexane and ethyl acetate (0.77 g, m.p. 162-164° C.) The product was identified by NMR spectroscopy and mass spectrometry.

Example VIII

Synthesis of Dye VII

**[0088]** To a solution of 3'-chloro-6'-(2-methylanilino)fluoran (3 g, 7 mmol) in sulfolane (10 mL) was added 2,6-lutidine (1.1 eq., 7.7 mmol, 0.83 g) followed by ZnO (0.8 eq., 5.6 mmol, 456 mg) and $ZnCl_2$ (3.0 eq., 21 mmol, 2.86 g). The solution was warmed to 100° C. and pyrrolidine (1.5 eq., 10.5 mmol, 747 mg) was added. After 1 hour the red solution was poured into water (500 mL), filtered and the collected solids were dissolved in ethyl acetate (500 mL). The organic extracts were washed with 0.5 N KOH (100 mL) and dried with magnesium sulfate. The solvent was removed under reduced pressure and the product purified by silica gel column chromatography (1:1 Hexanes/ethyl acetate→pure ethyl acetate gradient) to yield Dye VII (2.49 g, 5.25 mmol, 75%). The purified product, Dye VII, was crystallized from acetone/hexanes to yield 1.5 g of pink powder; m.p. 268° C. The product was identified by NMR spectroscopy and mass spectrometry.

Example IX Synthesis of Dye VIII

**[0089]** To a suspension of 3',6'-dichlorofluoran (184.5 g; 0.5 mol) in sulfolane (800 mL) was added $AlCl_3$ (3.0 eq., 200 g; 1.5 mol) and the mixture was warmed to 60° C. followed by the addition of 4-fluoro-2-methylaniline (68.8 g, 0.55 mol). The temperature of the orange solution was maintained at 80° C. for 10 minutes. Neat triethylamine (1.21 eq., 82.5 mL; 0.605 mol) was added dropwise with stirring over a period of 10 minutes. After stirring at 80° C. for four hours the completion of the reaction was followed by TLC of an aliquot (1:4 ethyl acetate:hexanes).

**[0090]** 2,6-Lutidine (2.2 eq., 127.9 ml; 1.1 mol) and pyrrolidine (39.10 g; 0.55 mol) were added to the warm reaction solution. The reaction mixture was stirred at 80° C. overnight. The reaction did not go to completion based on TLC even if extra 2,6-lutidine and pyrrolidine were added. The reaction mixture was cooled and then poured into ice/water (1.0 L) and stirred for 30 minutes and filtered. The filtrate was washed with of water (1.0 L).

**[0091]** The resulting paste was dissolved in dichloromethane (2.0 L) and washed with water. The organic layer was separated, dried over sodium sulfate and evaporated. The crude dye was purified by silica gel chromatography through a short plug. A gradient of ethyl acetate/hexane was used as eluent. The fractions containing pure product were combined, evaporated and recrystallized from acetone to give colorless crystals of Dye VIII (83 g; 33.7% yield, m.p. 283° C.). The product was identified by NMR spectroscopy and mass spectrometry.

Example X

Synthesis of Dye IX

**[0092]** To a suspension of 3',6'-dichlorofluoran (9.225 g, 25 mmol) in sulfolane (50 mL) was added $AlCl_3$ (3.0 eq., 10 g; 75 mmol) and the mixture was warmed to 60° C. followed by the addition of 4-Fluoro-2-methylaniline (3.44 g; 27.25 mmol). The temperature of the orange solution was maintained at 80° C. for 10 minutes. Neat triethylamine (1.1 eq., 3.75 ml; 27.25 mmol) was added dropwise with stirring over a period of 10 minutes. The reaction was stirred at 80° C. for 4 hours. The completion of the reaction was followed by TLC of an aliquot (1:4 ethyl acetate:hexanes).

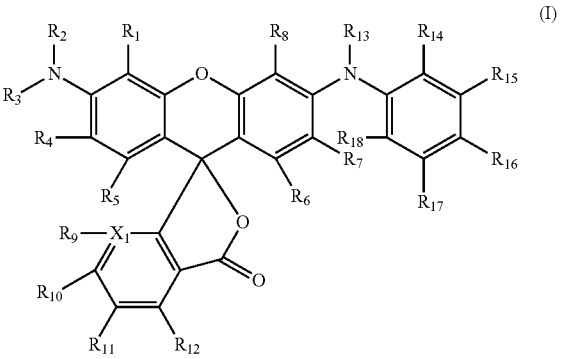
**[0093]** 2,6-Lutidine (2.0 eq., 7.85 ml; 50 mmol) and 2-methylpyrrolidine (2.32 g; 27.25 mmol) were added to the warm reaction solution. The reaction mixture was stirred at 80° C. overnight. The reaction did not go to completion based on TLC even when extra 2,6-lutidine and 2-methylpyrrolidine were added. The reaction mixture was cooled and then poured into ice/water (500 ml), stirred for 30 min, filtered and washed with water (100 mL).

**[0094]** The resulting paste was dissolved in 400 ml of dichloromethane and washed with water. The organic layer was separated, dried over sodium sulfate and evaporated. The crude dye was purified by silica gel chromatography. A gradient of ethyl acetate/hexanes was used as eluent. The fractions containing pure product were combined, evaporated and recrystallized from a mixture of acetone/hexanes to give colorless crystals of Dye IX (4.12 g, 32.54% yield, m.p. 228° C.). The product was identified by NMR spectroscopy and mass spectrometry.

**[0095]** Although the invention has been described in detail with respect to various preferred embodiments, it is not intended to be limited thereto, but rather those skilled in the art will recognize that variations and modifications are possible which are within the spirit of the invention and the scope of the appended claims.

We claim:

**1**. A compound represented by the formula




wherein:

$R_1$, $R_3$, $R_4$, $R_5$, $R_6$, $R_7$, $R_8$ and $R_{14}$ are each independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocycloalkyl, substituted heterocycloalkyl, alkoxy, substituted alkoxy, substituted carbonyl, acylamino and halogen;

$R_2$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocycloalkyl and substituted heterocycloalkyl;

or

$R_2$ and $R_3$ taken together with the nitrogen atom to which they are attached form a substituted or unsubstituted saturated heterocyclic ring system;

$R_9$ is absent or selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocycloalkyl, substituted heterocycloalkyl, alkoxy, substituted alkoxy, substituted carbonyl, halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, amino, substituted amino, alkylamino, substituted alkylamino, arylamino and substituted arylamino;

$R_{10}$, $R_{11}$ and $R_{12}$ are each independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocycloalkyl, substituted heterocycloalkyl, alkoxy, substituted alkoxy, substituted carbonyl, halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, amino, substituted amino, alkylamino, substituted alkylamino, arylamino and substituted arylamino;

$R_{13}$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocycloalkyl and substituted heterocycloalkyl;

$R_{14}$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocycloalkyl and substituted heterocycloalkyl;

or

$R_{13}$ and $R_{14}$ taken together with the atoms to which they are attached form a 5- or 6-membered heterocyclic ring;

$R_{15}$, $R_{16}$, $R_{17}$ and $R_{18}$ are each independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocycloalkyl, substituted heterocycloalkyl, alkoxy, substituted alkoxy, substituted carbonyl, halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, amino, substituted amino, alkylamino, substituted alkylamino, arylamino and substituted arylamino; and

$X_1$ is carbon or nitrogen;

provided that only one of $R_2$ and $R_{13}$ is hydrogen.

**2**. A compound as defined in claim **1** wherein $R_2$ and $R_3$ taken together form a pyrrolidine ring, $R_{10}$, $R_{11}$ and $R_{13}$ each is hydrogen, $X_1$ is carbon and $R_1$, $R_4$, $R_5$, $R_6$, $R_7$, $R_8$, $R_9$, $R_{12}$, $R_{14}$ and $R_{15}$-$R_{18}$ are as defined in claim **1**.

**3**. A compound as defined in claim **1** wherein $R_2$ is hydrogen, $R_3$ is alkyl, $R_{10}$ and $R_{11}$ are each halogen, $R_{13}$ is alkyl, $X_1$ is carbon and $R_1$, $R_4$, $R_5$, $R_6$, $R_7$, $R_8$, $R_9$, $R_{12}$, $R_{14}$ and $R_{15}$-$R_{18}$ are as defined in claim **1**.

**4**. A compound as defined in claim **1** wherein $R_1$, $R_4$, $R_5$, $R_6$, $R_7$, $R_8$, $R_9$ and $R_{12}$ are each hydrogen; $R_2$ is hydrogen or alkyl having from 1-18 carbon atoms, $R_3$ is alkyl having from 1-18 carbon atoms, or $R_2$ and $R_3$ taken together with the nitrogen atom to which they are attached form a pyrrolidine ring; $R_{10}$ and $R_{11}$ are each independently hydrogen or halogen; $R_{13}$ is hydrogen or alkyl having from 1-18 carbon atoms, $R_{14}$ is hydrogen or alkyl having from 1-18 carbon atoms, $X_1$ is carbon and $R_{15}$-$R_{18}$ are each independently hydrogen, alkyl having from 1-18 carbon atoms, or halogen.

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