United States Patent [19]

Khanna et al.

[11] **4,351,760**

[45] **Sep. 28, 1982**

[54] **NOVEL ALKYL SUBSTITUTED FLUORESCENT COMPOUNDS AND POLYAMINO ACID CONJUGATES**

[75] Inventors: **Pyare Khanna**, Mountain View; **Edwin F. Ullman**, Atherton, both of Calif.

[73] Assignee: **Syva Company**, Palo Alto, Calif.

[21] Appl. No.: **73,158**

[22] Filed: **Sep. 7, 1979**

[51] **Int. Cl.**[3] **A61K 39/385**; A61K 39/44; C07G 7/00

[52] **U.S. Cl.** ..... **260/112 R**; 23/230 B; 260/112 B; 260/112.5 R; 260/112.7; 260/121; 424/8; 424/12; 424/85; 424/88; 435/7; 435/188; 525/420; 549/388

[58] **Field of Search** ..... 260/112 R, 112 B, 121; 424/85, 88; 435/188; 525/420

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,174,384	11/1979	Ullman et al.	260/112 R
4,193,983	3/1980	Ullman et al.	260/112 B
4,220,450	9/1980	Maggio	424/12 X
4,230,805	10/1980	Singh et al.	260/112 R
4,318,846	3/1982	Khanna et al.	260/121 X

Primary Examiner—Howard E. Schain
Attorney, Agent, or Firm—Bertram I. Rowland

[57] **ABSTRACT**

Fluorescent antigen conjugates are provided comprising antigens covalently bonded to at least one 2,7-dialiphatic substituted-9-phenyl-6-hydroxy-3H-xanthen-3-one, wherein the 1- and 8-positions are unsubstituted. Also provided are novel fluorescent compounds absorbing at wavelengths in excess of 500 nm, having active functionalities for linking to the antigen. Finally, methods are provided for analyzing antigens in serum, whereby serum interference is avoided.

7 Claims, No Drawings

NOVEL ALKYL SUBSTITUTED FLUORESCENT COMPOUNDS AND POLYAMINO ACID CONJUGATES

BACKGROUND OF THE INVENTION

1. Field of the Invention

Fluorescent compounds find a wide variety of applications. They find use in fluorescent immunoassays, histochemical staining, displays, inks, and the like. Of particular interest for the subject invention is the use of antigenic conjugates (includes receptor conjugates) with fluorescent compounds to be used in the determination of a variety of ligands, both antigens and receptors. A substantial proportion of the ligands are assayed in physiological fluids, such as serum, where the serum can provide substantial background fluorescence. One way to diminish the background fluorescence resulting from naturally present fluorescers is to provide a fluorescent compound which absorbs at relatively long wavelengths. The compound should desirably have a large Stokes shift, be stable under conditions of the assay, be relatively free of non-specific interference, both from materials in solution and the compound to which the fluorescer is conjugated and to provide high quantum yields. In addition, for certain applications, it is desirable that the fluorescer be coupled with a quencher molecule, that is a molecule which is capable of absorbing the energy of the fluorescer in the excited state when within a predetermined distance, so that the fluorescer does not fluoresce.

2. Description of the Prior Art

A large number of fluorescein derivatives have been reported in the literature. The following are believed to be the most exemplary in relation to the subject invention and are reported in conjunction with the Chemical Abstracts citation. The numbering is based on the parent molecule 3',6'-dihydroxyspiro [isobenzofuran-1(3H),9'-(9H)xanthen]-3-one.

2',7'-di(n-hexyl) or di(n-heptyl)-4', 5'-dibromo-4,7-dichloro- are reported as being prepared, C.A. 31, 1621; 2',7'-di(n-hexyl)-, C.A. 31, 1621; 2',7'-di(alkyl)-; C.A. 31, 1388; 2',7'-diethyl or 2',7'-dibutyl-, C.A. 27, 5056; 2',7'-dimethyl-, C.A. 83, 18972s; 2',4',5',7'-tetrabromo-5 or 6-carboxy, C.A. 63, 13210h.

SUMMARY OF THE INVENTION

The subject compounds include novel fluorescent conjugates with members of specific binding pairs, ligands and receptors, as well as the fluorescent precursors to the conjugates. The conjugates find a wide variety of uses, particularly as reagents in immunoassays. The compounds are 2,7-dialiphatic-6-hydroxy-3H-xanthen-3-ones, normally having at least two chloro substituents, with the precursors having a linking group or functionality on a group, either aliphatic or aromatic, bonded to the 2- or 9-position of the xanthene.

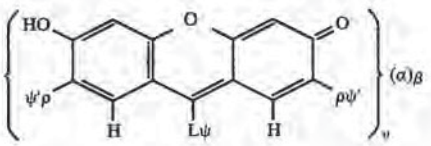
DESCRIPTION OF THE SPECIFIC EMBODIMENTS

The subject invention concerns fluorescent compounds, which are analogs of fluorescein, being particularly 2,7-dialiphatic substituted-9-substituted-6-hydroxy-3H-xanthen-3-ones, usually having at least two chloro substituents at other than the 1,8-positions and having a functional group for linking to a member of a specific binding pair bonded to a hydrocarbon group substituted at the 2- or 9-position, particularly 9-position, as well as the conjugates of the fluorescent compound to the member of the specific binding pair. The conjugates find particular use as reagents in assays for members of specific binding pairs.

The fluorescent precursors will have at least about 15 carbon atoms, usually 21 carbon atoms, and usually not more than about 40 carbon atoms, usually having from about 22 to 36 carbon atoms. There will preferably be at least two chlorine groups at other than the 1,8-positions and may be as many as 6 chlorines. In addition to chlorine, the only other heteroatoms are bromine, chalcogen, particularly oxygen and sulfur, and nitrogen, there being at least 4 heteroatoms and usually not more than 20 heteroatoms, more usually not more than about 16 heteroatoms and preferably not more than about 12 heteroatoms. Of the heteroatoms other than chlorine, there will be at least 3 oxygens, more usually at least 5 oxygens, and other than the oxygens which are part of the xanthene chromophore, are oxygens as non-oxo-carbonyl or oxy, particularly acid, ester or ether (normally bonded solely to carbon and hydrogen); sulfur is normally present as sulfonyl, thioether or mercapto; while nitrogen is normally present as amino or amido (bonded solely to carbon and hydrogen).

The fluorescent compounds are further characterized by having absorption maxima in 0.05 M phosphate buffer pH8 of at least about 500 nm, an extinction coefficient in the same medium of at least about 65,000, more usually at least 70,000 and a Stokes shift in the same medium of at least about 10 nm, more usually at least about 12 nm.

The 9-substituted-2,7-dialkylsubstituted xanthenes of this invention will for the most part have the following formula:



wherein:

ρis an aliphatic group, normally aliphatic hydrocarbylene (composed solely of carbon and hydrogen), saturated or unsaturated, branched or straight chain, particularly alkylene, more particularly $(CH_2)_\epsilon$, wherein ϵ is of from 1 to 12, usually 1 to 6, more usually 1 to 4; ρ is normally of from 1 to 12, usually 1 to 6, more usually 1 to 4 carbon atoms;

the two ψ's are the same or different, normally being the same, except when linking to α, and are hydrogen, a non-oxo-carbonyl functionality or one of the ψ's may be a non-oxo-carbonyl linking functionality;

L is a bond or divalent radical, usually an organic radical, of at least one carbon atom and not more than 20, usually not more than 16, more usually not more than 10 carbon atoms, normally having an aliphatic or aromatic hydrocarbon chain, or combination thereof, wherein the aliphatic chain is usually of from about 2 to 6 carbon atoms and the aromatic chain is of from about 6 to 12, usually 6 to 10 carbon atoms; L normally has from 0 to 4, when aromatic, usually 1 to 4, more usually 2 to 4 substituents, wherein the substituents may be halo, particularly chloro; non-oxo-carbonyl; thio, including inert sulfur acids, esters and amides; amino, particularly tert-amino or amido; and oxy, wherein the

substituents are normally of from 0 to 4 carbon atoms, there being at least two carbon atoms between heteroatoms bonded to saturated carbon atoms;

α is an organic compound, a member of a specific binding pair, either a ligand or receptor;

β is 1, when α is covalently bonded to ψ or ψ', and is otherwise 0; the covalent bond normally involves an amido, methylene sec-amino, ether, thioether or azo link;

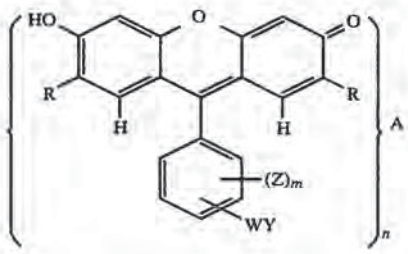
ψ is a group terminating in a heteroatom containing functionality when not bonded to α, wherein the terminal heteroatom containing functionality may be bonded directly to a carbon atom of L or through an oligomer of from 1 to 4 units, each unit of 1 to 4, usually 2 to 4 carbon atoms, which units are amino acids, alkyleneamino, or alkyleneoxy groups; the terminal functionality is normally oxo, including oxo-carbonyl and non-oxo-carbonyl; amino; oxy; thio; or active halogen; particularly non-oxo-carbonyl; and

ν is one when β is 0 and is otherwise on the average at least one and not more than the molecular weight of α divided by 500, usually divided by 1,000.

Desirably, there are from 2 to 6 chloro substituents on the fluorescent group (in the brackets), bonded at other than the 1,8-positions of the xanthenone. Also, the 4,5-positions may be unsubstituted or one or both, usually both, substituted with bromo, chloro, or alkyl of from 1 to 6, usually 1 to 3 carbon atoms.

The fluorescer compound or conjugate with the organic compound (α) may be linked, covalently or non-covalently to a support. The conjugate may be bound either through the fluorescer or organic compound. The support will be described in greater detail subsequently.

For the most part, the compounds of this invention having a 9-phenyl will have the following formula:



wherein:

R is an aliphatic group of from 1 to 8, usually 1 to 6, more usually 1 to 4, and preferably 1 to 3 carbon atoms, which may be substituted or unsubstituted, aliphatically saturated or unsaturated, particularly alkyl or carboxyalkyl of from 1 to 6, usually 1 to 4 carbon atoms;

Z is carboxy;

W is a bond or divalent radical having from 0 to 16, either 0 or usually 1 to 16 carbon atoms, more usually 1 to 8 carbon atoms and from 0 to 10, usually 2 to 8 heteroatoms, which are chalcogen (oxygen and sulfur) or nitrogen, wherein chalcogen is present bonded solely to carbon (oxy or oxo) and nitrogen is present bonded solely to carbon and hydrogen (amino and amido); carbon is normally aromatic or aliphatic, particularly free of aliphatic unsaturation, having from 0 to 2 sites of ethylenic unsaturation; W is conveniently a monomer or oligomer of units of from 1 to 4 carbon atoms e.g. alkylene, aminoacid, oxyalkylene, aminoalkylene, etc.;

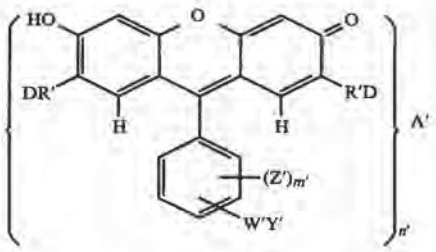
Y may be taken together with A to form an active functionality capable of forming a covalent bond with a heterofunctionality, such as amino, hydroxy, mercapto; that is with those functionalities present on A, when A is not taken together with Y; such heterofunctionality as, oxo- and non-oxo-carbonyl, oxy, thio, amino, active halo, active olefin, inorganic acyl group e.g. sulfonyl, etc. or acts as a linking functionality, being either methylene or heteroatom containing;

A, when not taken together with Y, is a member of a specific binding pair, which is ligand or receptor, wherein the ligand may be haptenic or antigenic, normally being of from about 125 molecular weight to an indefinite upper limit, although for the most part, most ligands will be under 10 million molecular weight, more usually under 2 million molecular weight, with varying ranges depending upon the nature of the ligand or receptor;

m will be 0 to 3, more usually 0 to 2; and

n will be 1 when Y and A are taken together and will otherwise be on the average 1 to the molecular weight of A divided by 500, more usually divided by 1,000, and more frequently divided by 2,000, wherein with specific binding pair members over 600,000 molecular weight A will normally be not greater than A divided by 5,000. In addition, there will usually be at least two chloro substituents bonded on any of the available positions where no specific atom is indicated. Also, the 4,5-positions may be substituted as described previously. Furthermore, either the conjugate or the fluorescer precursor may be bonded to a support of at least about 10,000 molecular weight and up to an indefinite molecular weight.

A preferred group of compounds will for the most part have the following formula:



wherein:

R' is alkylene of from 1 to 6, usually 1 to 4, and preferably 1 to 3 carbon atoms;

D is hydrogen or carboxy;

Z' is carboxy;

m' is 0 to 3, usually 0 to 2;

Y' may be taken together with A' to form an active functionality which may be non-oxo-carbonyl, including the sulfur analog thereof, amino bonded to at least one hydrogen atom, mercapto, active ethylene, usually having an α-carbonyl, halomethylcarbonyl, wherein halo is of atomic number 17 to 53, sulfonyl, or the like; when not taken together with A', Y' will be a linking functionality, either methylene or a heteroatom containing linking functionality, usually being an amide, ester, ether or azo link;

W' is a bond or linking group of from 1 to 16, usually 1 to 12, and preferably 1 to 8 atoms other than hydrogen, which are carbon, nitrogen, oxygen or sulfur, preferably carbon, nitrogen and oxygen, there being from 0

to 8 carbon atoms and 0 to 8 heteroatoms, with the number of carbon atoms and heteroatoms being at least 1, wherein nitrogen will be bonded solely to hydrogen and carbon, and will be either amino or amido, oxygen and sulfur will be bonded solely to carbon as oxy (thio) or oxo (thiono) and carbon is normally aliphatic and usually free of aliphatic unsaturation, generally having from 0 to 1 site of ethylenic unsaturation; W' may be alkylene or alkenylene of from 1 to 8, usually 1 to 4 carbon atoms, oxoalkylene or oxoalkenylene of from 1 to 8, usually 1 to 4 carbon atoms, imino (NH), N-formyl amino acid or N-formyl poly(amino acid) e.g. glycine or polyglycine, there being from about 1 to 4 amino acids, with the terminal carboxy being Y'A', or the like;

n' is 1 when Y' and A' are taken together and otherwise is on the average at least 1 to the molecular weight of A' divided by 500, usually divided by 1,000, more usually divided by 2,000, and when A' is over 500,000 molecular weight, more usually divided by 5,000;

there generally being not more than 5 carboxyl groups, usually not more than 4 carboxyl groups in total, and there being from 0 to 6 chloro groups, preferably 2 to 5 chloro groups bonded to available carbon atoms; and

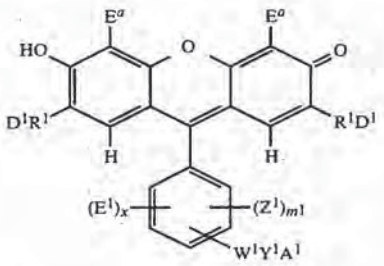
A' is a member of a specific binding pair, a ligand or receptor, wherein the ligand may be haptenic or antigenic, and haptenic ligands will include compounds of interest such as drugs, hormones, pollutants, compounds of interest in processing, agricultural chemicals, metabolites, and the like;

antigens will primarily be proteins, polysaccharides or nucleic acids, individually or in combination with each other or other materials, such as in cells, viruses, phage, or the like. The haptens will normally be from about 125 to 2,000, more usually to 1,000 molecular weight, while the antigens will normally be from about 2,000, more usually 5,000 molecular weight up to an indefinite molecular weight, usually not exceeding 10 million, more usually not exceeding 2 million.

The 4,5-positions are preferably unsubstituted or chloro-substituted.

In addition, the above conjugate may be bonded to a support. Various supports may be employed, both soluble or insoluble, swellable or nonswellable, by aqueous or organic solvents, naturally occurring or synthetic, organic or inorganic, porous or nonporous, or the like. Various polymeric materials include vinyl polymers and copolymers, polysaccharides, silicones, glass, carbon particles, such as graphite or charcoal, metals or metal compounds, poly(amino acids), nucleic acids or the like.

For the most part, the fluorescent compounds of the subject invention employed for conjugation will have the following formula:



wherein:

R^1 is alkylene of from 1 to 6, usually 1 to 4, preferably 1 to 2 carbon atoms;

D^1 is hydrogen or carboxy, preferably hydrogen;

Z^1 is carboxy;

E^a is hydrogen, alkyl of from 1 to 6, usually 1 to 3 carbon atoms, or chloro;

E^1 is chloro;

W^1 is a bond or linking group of from 1 to 12, usually 1 to 8 atoms other than hydrogen, and generally 1 to 8, usually 1 to 6 atoms in the chain wherein the atoms are carbon, nitrogen, oxygen and sulfur, particularly carbon, nitrogen and oxygen, wherein the carbon is aliphatic, the nitrogen is present as amido or amino, particularly amino bonded solely to carbon, and oxygen and sulfur are bonded solely to carbon and are oxy or oxo or the sulfur analogs thereof;

W^1 will generally be aliphatic, being saturated or unsaturated, normally saturated, having from 0 to 1 site of ethylenic unsaturation, alkylene or alkenylene of from 1 to 8, usually 1 to 4 carbon atoms, N-formyl amino acid or N-formyl poly(amino acid), where the terminal carboxy is derived from Y^1A^1, amino, mercapto, or the like;

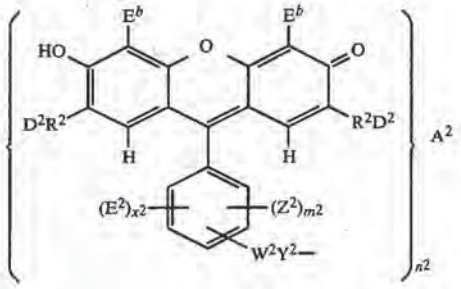
Y^1A^1 are taken together to form a functionality for linking, wherein Y^1A^1 are bonded solely to carbon or nitrogen, with the proviso that when Y^1 and A^1 are bonded to nitrogen, Y^1A^1 are carbonyl, including the nitrogen and sulfur analogs thereof and can be doubly bonded to nitrogen;

Y^1A^1 can be non-oxo-carbonyl, haloacetyl, halogen of atomic no. 9 to 53, particularly chloro or bromo, maleimido, mercapto, amino, or inorganic acyl, having phosphorous or sulfur as the central atom;

m^1 is 0 to 3, usually 0 to 2, there usually being not more than a total of 5 carboxyl groups in the molecule, usually not more than a total of 4 carboxyl groups, and preferably not more than about 2 carboxyl groups, other than Y^1A^1;

x is 0 to 4, preferably 2 to 4, there generally being not more than a total of 6 chloro groups in the molecule, usually not more than a total of 4 chloro groups, wherein x plus m^1 is not greater than 4.

For the most part, the compositions of this invention when bonded to ligand or support will have the following formula:



wherein:

E^b is hydrogen or chloro;

E^2 is chloro;

Z^2 is carboxy;

R^2 is alkylene of from 1 to 6, usually 1 to 3, preferably 1 to 2 carbon atoms;

D^2 is hydrogen or carboxy, preferably hydrogen;

W^2 is a bond or linking chain, when a linking chain being of from 1 to 12, usually of from 1 to 10, and pref-

erably of from about 1 to 8 atoms other than hydrogen, having from about 1 to 10, usually from about 1 to 8, and preferably from about 1 to 6 atoms in the chain or spacer arm, wherein the atoms are carbon, oxygen, nitrogen and sulfur, particularly carbon, oxygen and nitrogen in the spacer arm, wherein oxygen and sulfur are bonded solely to carbon, as oxy or oxo, and nitrogen is bonded solely to carbon and hydrogen, namely amino and amido, wherein heteroatoms bonded to saturated carbon atoms are separated by at least two carbon atoms;

W^2 is particularly alkylene, carboxamidoalkylene, wherein alkylene is of from about 1 to 2 carbon atoms-$(—CONHC_{1-2}—)_a$, wherein a is in the range of from about 1 to 4, usually 1 to 3;

Y^2 is non-oxo-carbonyl, carbamyl, thiocarbamyl, methylene, amino, or thio, particularly a functionality having a non-oxo-carbonyl group or sulfur analog thereof;

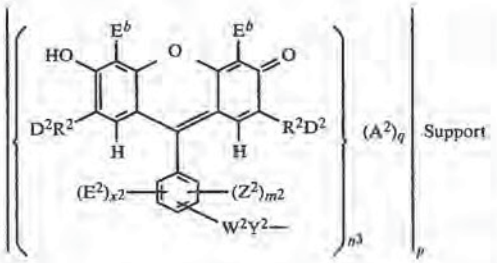
x^2 is 0 to 4;

m^2 is 0 to 3, preferably 1 to 2;

n^2 is 1 to the molecular weight of A^2 divided by 500, usually divided by 1,000, more usually divided by 2,000, wherein when A^2 is a ligand of between about 125 to 2,000 molecular weight, n^2 will generally be of from about 1 to 20, when A^2 is a ligand of from about 2,000 to 600,000 molecular weight, n^2 will generally be in the range of about 1 to 100, more usually in the range of about 2 to 50; and

A^2 is a ligand of at least about 125 molecular weight and may be 10 million or more molecular weight, which is haptenic or antigenic, wherein haptens are from about 125 to 2,000 molecular weight and antigens will generally range from about 5,000 to 10 million molecular weight, more usually from about 5,000 to 2 million molecular weight and frequently from about 5,000 to 600,000 molecular weight, the ligand being a member of a specific binding pair, which comprises a compound having at least 1 determinant or epitopic site and a receptor which is capable of recognizing the determinant site or A^2 is a receptor of from about 10,000 to 1 million molecular weight.

Finally, in some instances it may be desirable to have the fluorescent compound or the conjugate of the fluorescent compound with ligand, bonded to a support, where the linkage may be derived from either the fluorescent compound or the ligand, normally the ligand. In this situation, the linking group may be any convenient functionality which is present on the fluorescent compound or the ligand or a functionality which may be introduced, particularly on the ligand. These compositions will for the most part have the following formula, where the symbols are derived from the previous formula for the conjugate for the most part:



wherein:

all of the symbols have been defined previously, except for:

n^3 which is at least 1 and up to the molecular weight of A^2 divided by 500, usually 1000, more usually 1,500, with the proviso that when q is 0, n^3 is 1;

q which is 0 or 1;

p which is at least 1 and of up to the molecular weight of the support divided by 500, more usually the molecular weight of the support divided by 1,000, wherein when the molecular weight of the support exceeds 500,000, p will normally be not greater than the molecular weight of the support divided by 5,000, more usually divided by 10,000; and

Support intends a macromolecular support of at least about 10,000 molecular weight, which may be naturally occurring or synthetic, having a plurality of functionalities for linking e.g. carboxy, hydroxy, or amino, usually being a polymer, such as a polysaccharide or an addition polymer; the support being bonded to the conjugate by any convenient functionality remaining on A^2 or the conjugate in the brackets, the particular manner of linking not being a significant aspect of the subject invention. For example, if A^2 is a poly(amino acid), carboxylic groups on the support can be used for amide formation or maleimide groups may be introduced and linked to mercapto groups.

Quite obviously, the compounds of the subject invention can be modified so as not to be within the above formulas, without significantly affecting the properties of the compounds. For example, one or more of the acidic anionic groups could be esterified or amidified, or alkyl groups can be substituted on the phenyl, as well as other groups, such as cyano, nitro, or the like. However, these changes will in most cases require additional synthetic steps which are not warranted by the degree of enhancement, if any, in the spectroscopic or chemical properties of the resulting product.

Turning now to a consideration of the individual components of the subject compositions, the fluorescein derivatives will be considered first. The following is a list of illustrative fluorescein derivatives coming within the scope of the subject invention.

TABLE I

2,7-dimethyl-4,5-dichloro-9-(2′,4′,5′-tricarboxyphenyl)-6-hydroxy-3-xanthen-3-one

2,7-diethyl-4,5-dichloro-9-(2′,4′,5′-tricarboxy-3′,6′-dichlorophenyl)-6-hydroxy-3H-xanthen-3one

2,7-dihexyl-9-(2′,4′,5′-tricarboxyphenyl)-6-hydroxy-3H-xanthen-3-one

2,7-dimethyl-4,5-dichloro-9-(2′-carboxy-4′-isothiocyanato-3′,5′-dichlorophenyl)-6-hydroxy-3H-xanthen-3-one

2,7-dimethyl-9-(2′-carboxy-4′-isocyanato-3′,5′,6′-trichlorophenyl)-6-hydroxy-3H-xanthen-3-one

2,7-dimethyl-9-(4′-carboxy-5′-carboxylphenyl)glycylglycylglycine amide-6-hydroxy-3H-xanthen-3-one

2,7-di(carboxymethyl)-9-(4′,5′,-dicarboxy-2′,3′,6′-trichlorophenyl)-6-hydroxy-3H-xanthen-3-one

2,7-di(carboxypropyl)-4,5-dichloro-9-(3′,4′-dicarboxyphenyl)-6-hydroxy-3H-xanthen-3-one

2,7-diethyl-9-(2′-carboxy-4′-amino-3′,5′-dichlorophenyl)-6-hydroxy-3H-xanthen-3-one

2,7-dimethyl-9-(2′-carboxy-4′-mercaptophenyl)-6-hydroxy-3H-xanthen-3-one

2,7-dimethyl-9-(2′-carboxy-4′-carboxymethylphenyl)-6-hydroxy-3H-xanthen-3-one

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.