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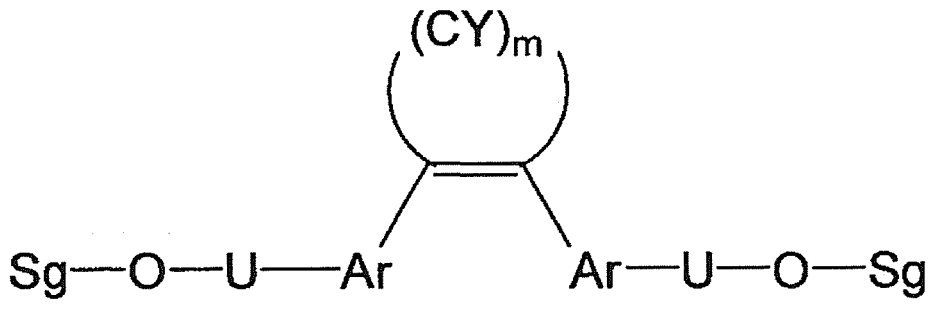
(54) **WATER-SOLUBLE PHOTOCHROMIC MOLECULE**

(57) A diarylethene compound having high water-solubility is provided, and the compound is a diarylethene compound of formula (I)

[Formula 1]



(I)

wherein, Sg is a monovalent sugar-type residue consisting of a sugar-type compound (in which some of hydroxyl groups may be protected) selected from a group consisting of a six-membered ring sugar, a five-membered ring sugar, cyclitol and oligosaccharides containing a six-membered ring sugar, a five-membered ring sugar, or cyclitol and excluding an hydroxyl group;
U is $-(CH_2)n-$, $-CH_2-U'-$, or $-C(=O)-$ (wherein, n is an integer of 1 to 5, U' is a C1-C10 alkyl group binding to Ar); and
Ar is a group represented by formula (A1) or (A2);

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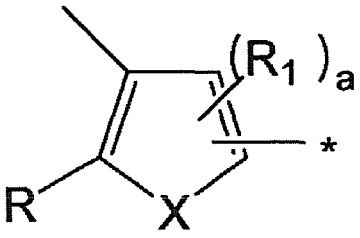
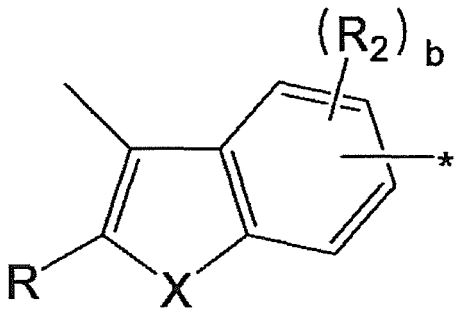
(Cont. next page)

[Formula 2]



(A 1)



(A 2)

wherein,
X is S, SO_2, NR_3 (R_3 is a C1-C3 alkyl group) or O,
R is C1-C4 alkyl group,
R_1 and R_2 are independently a C1-C3 alkyl group,
a is 0 or 1, b is an integer of 0-3, and
* represents a bond with U);
Y is a hydrogen atom or a halogen atom;
m is an integer of 5-7.

Description

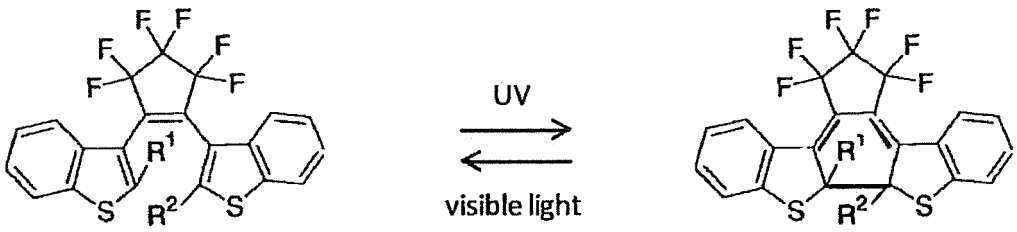
TECHNICAL FIELD

[0001] The present invention relates to a water-soluble photochromic molecule, and more specifically to a water-soluble diarylethene compound.

BACKGROUND ART

[0002] Photochromic molecules are molecules that reversibly transform between two isomers with different absorption spectra while maintaining the same molecular weight when irradiated with appropriate wavelength of light. The diarylethene compound is known to exhibit excellent photochromic performance (Non-Patent Document 1). The diarylethene has a following structure, and it undergoes cyclization/cycoreversion reactions upon irradiation with light as shown in the following scheme.

[Formula 1]



[0003] Ext ensive studies have been carried out to apply the photochromic molecules as optical memory media that can optically store information (Patent Document 1, etc.). In such use, the media were prepared by dissolving photochromic molecules in an organic solvent, then spreading the resulting solution over a substrate.

[0004] Recently, bioimaging using fluoresnent microscope, which is a method to observe an image by binding fluorochrome molecules to biomolecules, has been actively studied. Bioimaging that employs green fluorescent proteins (GFP) is frequently used, but this method is disadvantageous in that the label molecule is large, and the protein-protein interaction affects the target biomolecule. Diarylethenes are expected to achieve bioimaging with high resolution, since they are low molecular weight compounds. However, it is indispensable to provide water-solubility to the compounds for the application to biological samples.

[0005] In the studies of optical memory media mentioned above, the diarylethene compound did not need to be dissolved in water, so Patent Document 1 does not mention anything about a water-soluble diarylethene compound. Concerning water-solubility, Non-Patent Documents 3, 4 teach diarylethene compounds that have ionic groups or amphiphilic groups. However, these compounds tend to be aggregated in water, and would excessively affect the target molecule due to their strong ionic interaction, so they are hardly applied to bioimaging. Under such situation, a highly water-soluble diarylethene compound obtained by a different means was desired.

CITATION LIST

PATENT DOCUMENTS

[0006] Patent Document 1: Japanese Publication No. 2005-325087

NON-PATENT DOCUMENTS

[0007]

Non-Patent Document 1: M. Irie et al., Nature, 420, 759 (2002)
Non-Patent Document 2: K. H. Jones and J. A. Senft, J. Histochem. Cytochem., 33, 77 (1985)
Non-Patent Document 3: M. Takeshita, et al., J.Org. Chem., 63, 9306 (1998)
Non-Patent Document 4: M. Matsuda, et al., Chem. Lett. 32,1178 (2003)
Non-Patent Document 5: S. Kobatake, et al., J. Am. Chem. Soc. 121, 2380 (1999)
Non-Patent Document 6: T. Yamaguchi, et al., J. Photochem. Photobio. A, 178, 162 (2006)

SUMMARY OF INVENTION

TECHNICAL PROBLEM

[0008] In view of the above situation, the object of the present invention is to provide a highly water-soluble diarylethene compound.

SOLUTION TO PROBLEM

[0009] The present inventors found that a diarylethene compound having sugar groups has good water-solubility, and completed the present invention. In other words, the above object is achieved by the present inventions shown below.

[1] A diarylethene compound represented by the following formula (I).
[2] A method for producing the diarylethene compound of [1] above comprising:

(1) a step of preparing a halogenated sugar derivative that is derived from a sugar-type compound selected from a group consisting of a six-membered ring sugar, a five-membered ring sugar, cyclitol and oligosaccharides containing a six-membered ring sugar, a five-membered ring sugar, or cyclitol, and that includes 1 hydroxyl group substituted with a halogen atom and all other hydroxyl groups protected by protection groups;
(2) an etherification step of reacting the halogenated sugar derivative with the compound represented by formula (a) to generate a compound represented by formula (b); and
(3) a deprotection step of removing the protection group of a compound represented by formula (b).

ADVANTAGEOUS EFFECTS OF INVENTION

[0010] The present invention can provide a diarylethene compound having a high water-solubility.

BRIEF DESCRIPTION OF DRAWINGS

[0011]

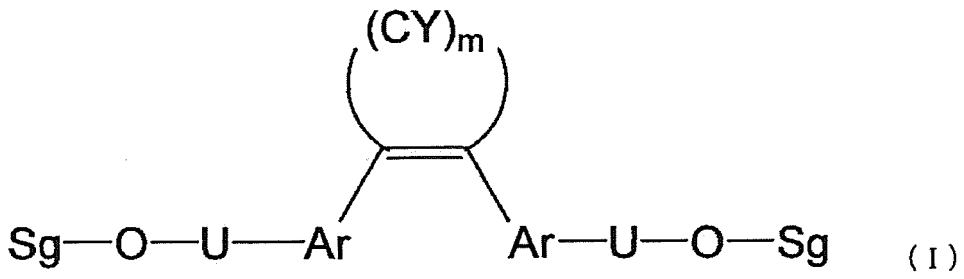
Figure 1 is a diagram showing the photochromic property of an aqueous solution of a compound of Example 1.
Figure 2 is a diagram showing the photochromic property of an aqueous solution of a compound of Example 2.
Figure 3 is a diagram showing the photochromic property of an aqueous solution of a compound of Example 3.
Figure 4 is a diagram showing the photochromic property of an aqueous solution of a compound of Example 4.
Figure 5 is a diagram showing the photochromic property of an-aqueous solution of a compound of Example 4.
Figure 6 is a diagram showing the fluorescent label property of a biological tissue. Figure 7 is a diagram showing the fluorescent label property of a biological tissue

DESCRIPTION OF EMBODIMENSTS

1. Diarylethene Compound

[0012] The diarylethene compound of the present invention is represented by formula (I).

[Formula 2]



(I)

(1) Sugar-Type Residue Sg

[0013] The compound has sugar-type residues Sg. Sugar-type residue is a group derived from sugar or a similar compound. Sg is a monovalent sugar-type residue consisting of a sugar-type compound excluding one hydroxyl group, the sugar-type compound being selected from a group consisting of a six-membered ring sugar, a five-membered ring sugar, cyclitol and oligosaccharides containing a six-membered ring sugar, a five-membered ring sugar, or cyclitol. Some of the hydroxyls in the sugar-type residue may be protected by protection groups. The sugar-type compound is referred to hereinafter as simply "sugar" and the sugar-type residue is referred to hereinafter as simply "sugar residue" for convenience.

[0014] A six-membered ring sugar is sugar with 6-membered ring structure, including glucopyranose, arabinopyranose, xylopyranose, lyxopyranose, allopyranose, altropyranose, mannopyranose, gulopyranose, idopyranose, galactopyranose, talopyranose, and glucuronic acid, without being limited thereby.

[0015] A five-membered ring sugar is sugar with 5-membered ring structure, including ribofuranose, arabinofuranose, xylofuranose, erythrofuranose, threofuranose, and lyxofuranose, without being limited thereby.

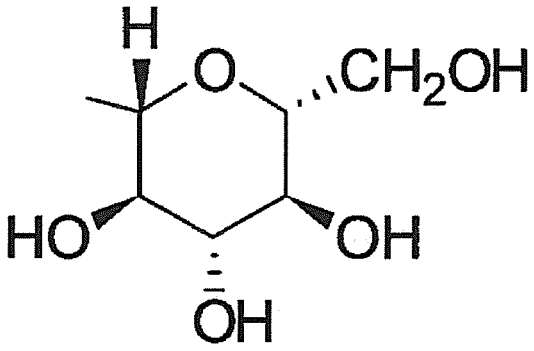
[0016] Cyclitol is a cycloalkane polyol (polyhydroxy cycloalkane), that is, a cyclic sugar alcohol, and it includes inositol as an example.

[0017] An oligosaccharide is a compound composed of about 2 to 15 units of compounds that are a six-membered ring sugar, a five-membered ring sugar, and a cyclitol sugar bound to each other by the glycoside linkage, etc. Examples of oligosaccharides include sucrose, raffinose, stachyose, trehalose, lactose, etc., without being limited thereby.

[0018] When availability is considered, a preferable sugar in the present invention is glucopyranose.

[0019] Sg is a monovalent sugar residue excluding a hydroxyl group from the above sugars. Any hydroxyl group can be removed, but a hydroxyl group bound to a carbon atom in the ring is preferable, and a hydroxyl group on the position-1 carbon atom (hemiacetal hydroxyl group) is more preferable. For example, a sugar residue of glucopyranose excluding the hemiacetal hydroxyl group is a glucosyl group, and it is represented by the following chemical formula.

[Formula 3]



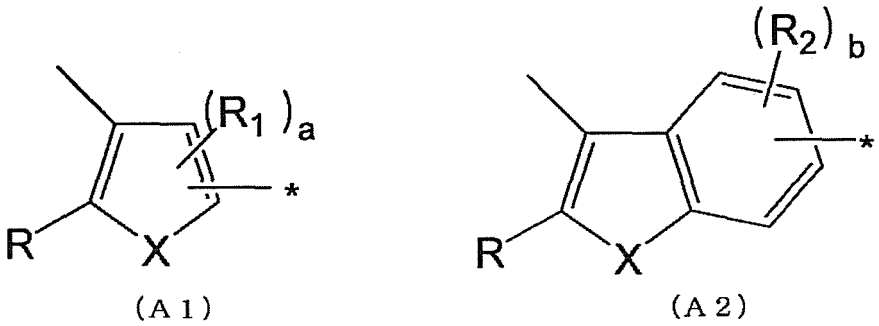
[0020] A glucosyl group may be either an α-glucosyl group, or a β-glucosyl group, but the β-glucosyl group is preferable from the viewpoint of reducing the steric hindrance.

[0021] Also, as mentioned above, some of the hydroxyl groups can be protected in the sugar residue. A more detailed explanation of the protection group will follow, but an acyl group, such as an acetyl group, is preferable. If there is a protection group, it should preferably exist in a number of 1 to 2, and more preferably 1 per 1 sugar residue.

(2) Aromatic Group Ar

[0022] Ar is an aromatic group represented by the following formula (A1) or (A2).

[Formula 4]



(A 1) (A 2)

[0023] X is S, SO_2, NR_3 (R_3 is a C1-C3 alkyl group), or O, of which S or SO_2 is preferable to obtain a good photochromic property. In particular, S is preferable as X in formula (A1), and S or SO_2 is preferable as X in formula (A2).

[0024] R is a C1-C4 alkyl group. In the present invention, the alkyl group includes chain-shaped and a branch-shaped groups. Hence, C1-C4 alkyl group is specifically a methyl group, an ethyl group, an n-propyl group, an i-propyl group, an n-butyl group, and a t-butyl group.

[0025] R_1, R_2 are independently C1-C3 alkyl groups. When we say "independently," it means that R_1, R_2 can be the same or they may differ. R_1 is a substituent at position-4 or position-5 of a 5 membered-ring in formula (A1). a is the number of R_1, which is either 0 or 1. The presence of R_1 may reduce the photochromic property, so R_1 should preferably not exist (i.e. a=0), but if it does exist, a less bulky R_1 provides a better photochromic property, so R_1 should preferably be a methyl group.

[0026] R_2 is a C1-C3 alkyl group, and it is a substituent at positions 4 to 7 of the heterocyclic ring in formula (A2). b is the number of R_2, which is an integer between 0 to 3. The presence of R_2 may reduce the photochromic property, so R_2 should preferably not exist (i.e. b=0), but if it does exist, b should preferably be 1 or 2, of which 1 is more preferable. If R_2 does exist, R_2 should preferably be a methyl group for the reason provided above.

[0027] In formula (A1), * indicates a linkage of the 5-membered ring with the linkage group U. To reduce the steric hindrance, the position-5 carbon atom of the 5 membered-ring should bind with U. If there is an R_1, it will bind to position-4. Similarly in formula (A2), * indicates a linkage of the benzene ring with the linkage group U. To reduce the steric hindrance, the position-6 carbon atom should bind with U.

(3) Linkage Group U

[0028] U is a linkage group to link Sg and Ar, and it is $-(CH_2)n-$, $-CH_2-U'-$, or $-C(=O)-$. n is an integer of 1 to 5. A large n may reduce the water-solubility of the diarylethene compound to be obtained, so n should preferably be 1 to 3, and more preferably 1.

[0029] U' is a C1-C10 alkyl group binding with Ar. The water-solubility of diarylethene compound may decrease for a large number of carbons, so the number of carbons should preferably be 1 or 2, and more preferably 1. As mentioned above, the alkyl group includes chain-shaped and branch-shaped groups.

(4) Ethene Unit

[0030] The $-(CY)_m-$ in formula (I) shows that the compound has an alicyclic structure. Y is a hydrogen atom or a halogen atom. To obtain a good photochromic property, Y should preferably be a halogen atom, and more preferably a fluorine atom. m is an integer of 5 to 7 and it should preferably be 5 for the same reason.

2. Production Method

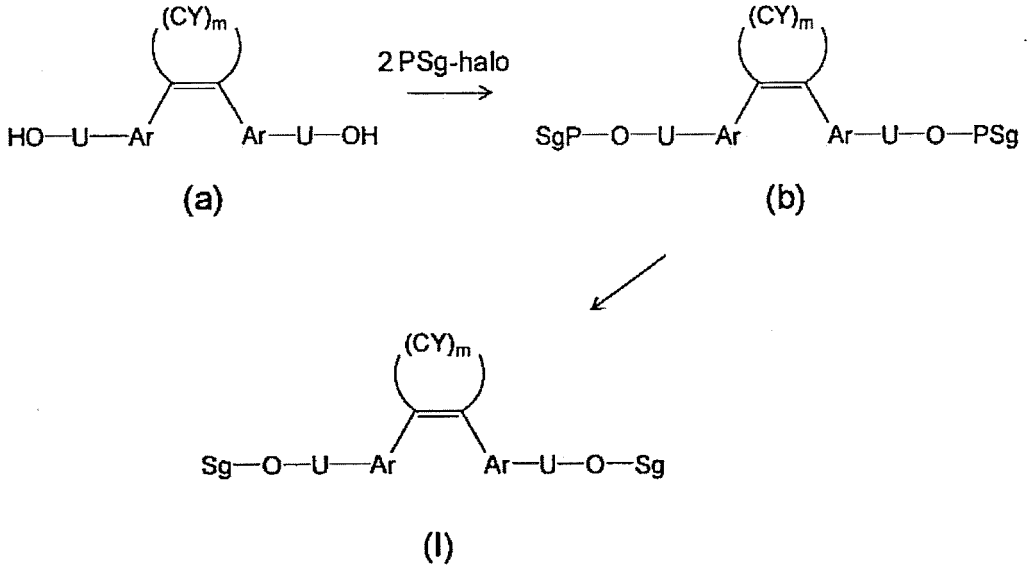
[0031] The diarylethene compound of the present invention is produced by any given method, but a preferable production method is provided below.

2-1. First Production Method

[0032] The present method includes:

(1) a step of preparing a halogenated sugar derivative that is derived from a sugar-type compound selected from a group consisting of a six-membered ring sugar, a five-membered ring sugar, cyclitol and oligosaccharides containing a six-membered ring sugar, a five-membered ring sugar, or cyclitol, and that includes 1 hydroxyl group substituted with a halogen atom, and all other hydroxyl groups protected by protection groups;
(2) an etherification step of reacting the halogenated sugar derivative with the compound represented by formula (a) to produce a compound represented by formula (b);
(3) a deprotection step of removing the protection group of a compound represented by formula (b).

[Formula 5]



[0033] A detailed explanation is provided below, and for the ease of understanding, an example will be provided in which the halogenated sugar derivative is acyl halogenated sugar, and the etherification step includes a glycosylation reaction.

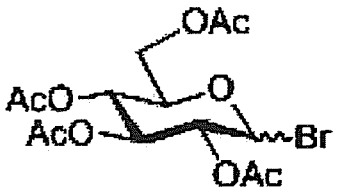
(1) Preparation Step of Acyl Halogenated Sugar (Preparation Step of Halogenated Sugar Derivative)

[0034] The acyl halogenated sugar used in the present invention is derived from a sugar selected from a group consisting of a six-membered ring sugar, a five-membered ring sugar, cyclitol and oligosaccharides containing a six-membered ring sugar, a five-membered ring sugar, or cyclitol, and it includes 1 hydroxyl group substituted with a halogen atom, and all other hydroxyl groups protected by protection groups. In the above scheme, the acyl halogenated sugar is represented by PSg-halo. The hydroxyl group substituting the halogen atom should preferably be the hydroxyl group on the anomer position.

[0035] A protection group is a group for protecting the hydroxyl group to prevent side reaction of the hydroxyl group in the sugar. In the present invention, the hydroxyl group can be protected by a group that is commonly used. Examples of such protection group includes an acyl group, an acetal group, and a silyl ether group. Among these, the acyl group is preferable since it is easy to deprotect, and an acetyl group is more preferable.

[0036] The acyl halogenated sugar can be prepared by a known method. For example, it can be produced by reacting pentaacetyl glucopyranose with HOAc-HBr (hydrogen bromide-acetic acid solution). The hydroxyl group on the anomer position (a hydroxyl group on the position-1 carbon atom) is normally halogenated. The above step can be performed by dissolving the protected sugar in a hydrogen bromide-acetic acid solution, then sealing it and reacting it for a day and a night. A preferable acyl halogenated sugar is represented by formula (s1) below.

[Formula 6]



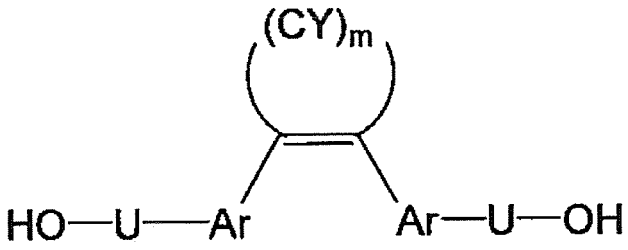
(s 1)

(2) Glycosylation Step (Etherification Step)

1) Diols Represented by Formula (a)

[0037] This step is a reaction of the acyl halogenated sugar and diols represented by formula (a).

[Formula 7]

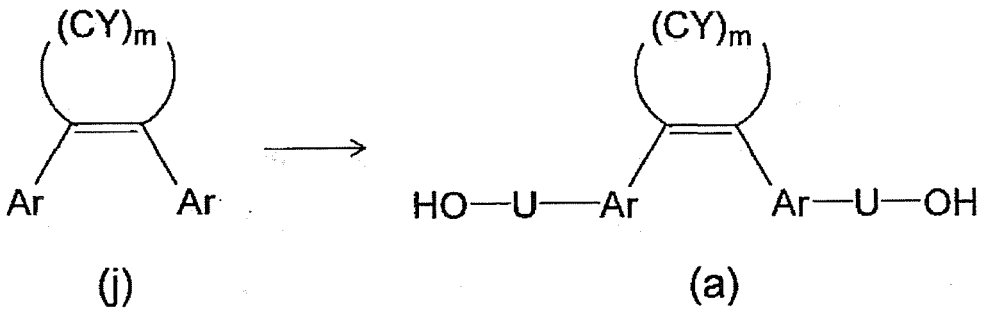


(a)

[0038] In formula (a), U, Ar, Y and m are as defined above. However, U in the present production method should preferably be $-(CH_2)n-$ or $-CH_2-U'-$.

[0039] The diol can be prepared by a known method. For example, a -U-OH group may be introduced in the aromatic group Ar of the diarylethene compound of formula (j) shown in the following scheme.

[Formula 8]



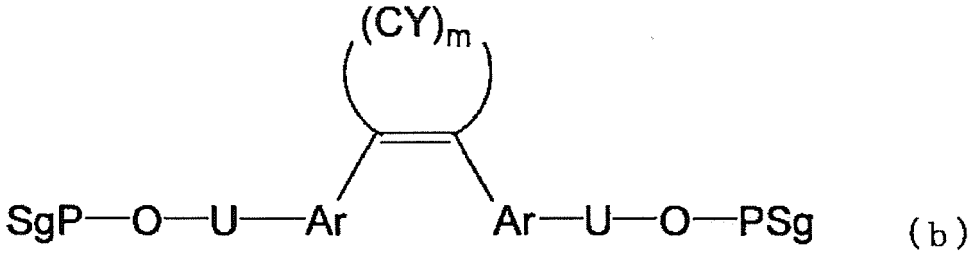
[0040] Specifically, the diarylethene compound of formula (j) and dichloromethylmethyl ether are reacted under the presence of $AlCl_3$, etc. to introduce a formyl group in the Ar group, and a reduction of the formyl group will provide a diol in which $-CH_2-OH$ is introduced as the -U-OH group.

[0041] The diarylethene compound of formula (j) whose Ar is a thiophene structure can be synthesized by the methods of Non-Patent Documents 5, 6. Further, an oxidation of S in a compound whose Ar is a thiophene structure produces a compound whose Ar is a thiophene sulfone structure.

2) Intermediate Represented by Formula (b)

[0042] A reaction of the diol of formula (a) and an acyl halogenated sugar induces a glycosylation reaction that generates an intermediate represented by formula (b).

[Formula 9]



(b)

[0043] In formula (b), U, Ar, Y and m are as defined above. PSg is a sugar residue of the Sg in which all hydroxyl groups are protected.

[0044] This reaction occurs by the detachment of a hydrogen atom of the compound of formula (a) and a halogen at the anomer position of the acyl halogenated sugar, so it should preferably be performed under the presence of a reaction accelerator that accelerates the detachment of the hydrogen atom and halogen. Examples of the reaction accelerator include silver oxide, such as Ag_2O, and mercury salts, such as $HgBr_2$, $Hg(CN)_2$. In the present invention, it is preferable to use Ag_2O, since it is more capable of accelerating reaction. The amount of Ag_2O to be used should preferably be 5 to 10 mols against 1 mol of a compound of formula (a).

[0045] In addition, the reaction can be further accelerated by also using a dehydrator. A known dehydrator can be used, but a dehydrator that can be easily removed, such as a molecular sieve, etc., is preferable. The amount of molecular sieve 4A to be used should preferably be 0.10 g/2 mL of the solvent.

[0046] The solvent to be used in the present step is not limited, but a solvent having low solubility to water is preferable, since removing water from the system further accelerates the reaction as mentioned above. An example of a preferable solvent includes a chlorine-type hydrocarbon, such as methylene chloride, and an aromatic hydrocarbon, such as toluene. In particular, a chlorine-type hydrocarbon is more preferable.

[0047] The reaction temperature is determined as necessary from the viewpoint of accelerating reaction and regulating side reaction. A temperature between 10 to 40°C is preferable in the present invention.

[0048] As mentioned above, it is preferable to use an acyl halogenated sugar that includes a halogenated hydroxyl group on the position-1 carbon atom and other hydroxyl groups protected for ease of synthesis or other reasons, but such acyl halogenated sugar has an α-isomer and a β-isomer. In the acyl halogenated sugar, the neighboring hydroxyl group on position-2 is protected by an acyl group, and the neighboring-group participation brings about a preferential generation of β-glucosyl isomer. So when the above acyl halogenated sugar of formula (s1) is used to obtain the compound of formula (a), the PSg in the obtained compound is a group derived from the β-glycosyl group.

(3) Deprotection Step

[0049] This step removes the protection group of the intermediate represented by formula (b). The protection group can be removed by a known method. For example, when the hydroxyl group is protected by an acyl group, such as an acetyl group, the protection group can be readily removed by reacting the protected hydroxyl group with alkali, such as lithium hydroxide, sodium hydroxide, potassium carbonate. It is preferable to use lithium hydroxide in the present invention, and it is more preferable for the amount of use to be 5 to 10 mol against 1 mol of the intermediate represented by formula (b).

[0050] The solvent to be used in the present reaction is not limited, but alcohol such as methanol is preferable. The reaction temperature is not limited, but a temperature of 10 to 30°C is preferable.

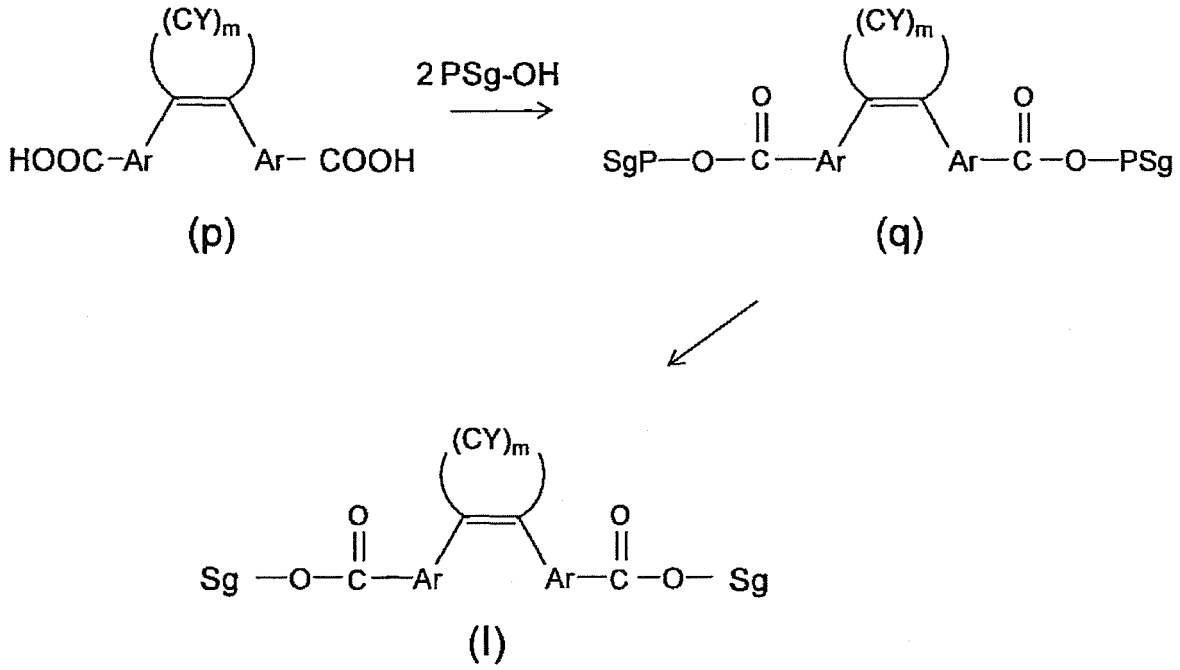
2-2. Second Production Method

[0051] The method comprises:

(1) a step of preparing a protected sugar compound selected from a group consisting of a six-membered ring sugar, a five-membered ring sugar, cyclitol and oligosaccharides containing a six-membered ring sugar, a five-membered ring sugar, or cyclitol, and all hydroxyl groups excluding one are protected by protection groups;
(2) an etherification step of reacting the protected sugar compound with the compound represented by formula (p) to generate a compound represented by formula (q);
(3) a deprotection step of removing the protection group of a compound represented by formula (p).

[0052] The protected sugar compound is referred to hereinafter simply as "protected sugar" for the reason mentioned above. The scheme of the method is shown below.

[Formula 10]



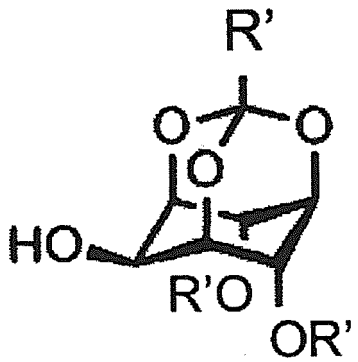
(1) Preparation Step of Protected Sugar

[0053] The protected sugar is shown as PSg-OH in the scheme. The protected sugar is a sugar that has all of its hydroxyl groups excluding one protected by protection groups. Those protection groups mentioned above can be used, but the group preferable in the present production method is the acetal group, and a more preferable group is the methoxymethyl group.

[0054] The protected sugar can be prepared by a known method. For example, it can be produced by introducing a protection group in sugar, such as furanose. All hydroxyl groups excluding the hydroxyl group on the anomer position (a hydroxyl group on the position-1 carbon atom) should preferably be protected.

[0055] Protected sugars preferable for use in the present invention include the compound represented by formula (s2) below. In formula (s2), R' is a methyl group or an ethyl group, and the methyl group is preferable, since it can easily be deprotected.

[Formula 11]



(s 2)

(2) Esterification Step

1) Dicarboxylic Acids Represented by Formula (p)

[0056] This step performs a reaction of a protected sugar and dicarboxylic acids represented by formula (p). In formula (p), Ar, Y and m are defined as shown above. The dicarboxylic acids can be prepared by a known method. For example, a dicarboxylic acid of formula (p) can be produced by introducing a formyl group to the aromatic group Ar of the diarylethene compound of formula (j) to obtain a diformyl, then oxidating the formyl group to produce a dicarboxylic acid of formula (p), as indicated in the first production method.

2) Intermediate Represented by Formula (q)

[0057] A reaction of the dicarboxylic acids of formula (p) and protected sugar generates intermediates represented by formula (q). In formula (q), Ar, Y, m and PSg are defined as shown above. The reaction is an esterification reaction, so it should be carried out under the presence of a known reaction accelerator. Examples of the reaction accelerator include a dehydrator, such as DCC. The amount of DCC to be used should preferably be 2 to 5 mols against 1 mol of the compound of formula (p).

[0058] The solvent to be used in the present step is not limited, but a removal of water from the system accelerates reaction as mentioned above, so a solvent having low water-solubility is preferable. The preferable solvents are as already mentioned above.

[0059] The reaction temperature is determined as necessary from the viewpoint of accelerating reaction and regulating side reaction. A temperature between 10 to 40°C is preferable in the present invention.

(3) Deprotection Step

[0060] This step removes the protection group of the intermediate of formula (q). The protection group can be removed by a known method. For example, when the protection group is an acetal group, deprotection can be carried out by an excessive amount of acid, such as chloride. The solvent to be used in the present reaction is not limited, but alcohol, such as methanol, is preferable. The reaction temperature should preferably be 10 to 30°C without being limited thereby.

[0061] As a result of the above steps, the target compound can be obtained. The obtained compound is represented by formula (I) and has a linking group U of -C(=O)-.

3. Usages and the Like

[0062] The diarylethene compound of the present invention is soluble in water or an aqueous solvent. In other words, in the present invention, the compound is water-soluble if it dissolves in water or in a water/organic solvent (mixed solvent) having water concentration of 70 wt% or higher, preferably 80 wt% or higher, and more preferably 90 wt% or higher.

[0063] Further, the diarylethene compound of the present invention contains sugar residues, so the sugar residues can be further modified to introduce labeling groups or enhance biocompatibility. Accordingly, the diarylethene compound of the present invention can be readily incorporated into biological sample to achieve bioimaging at a high resolution.

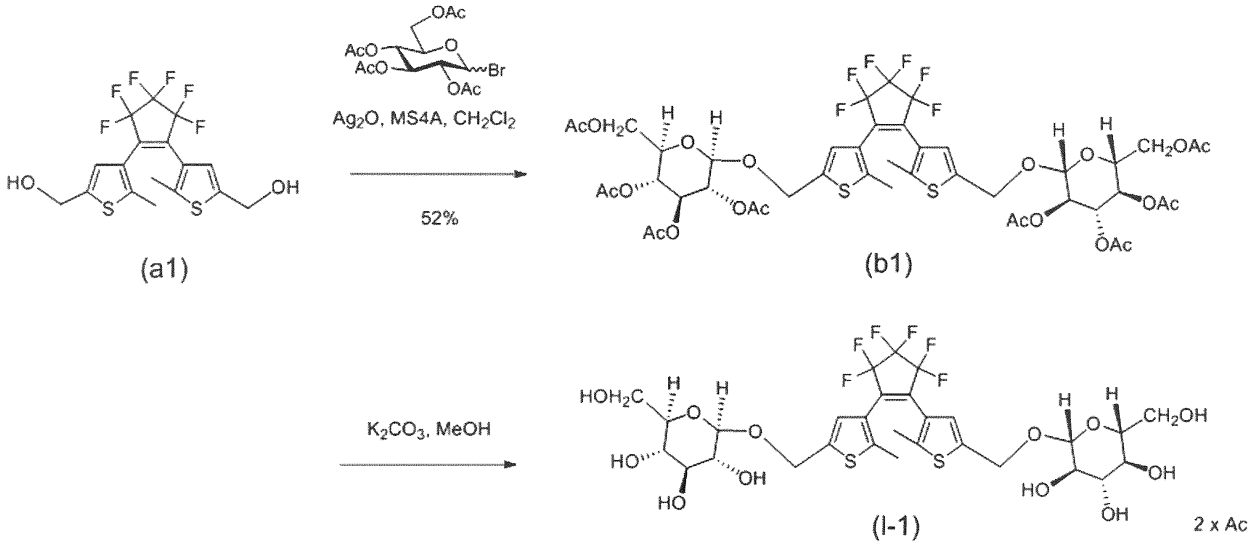
[0064] In addition, the diarylethene compound of the present invention can achieve high resolution bioimaging when used for super-resolution microscopy (PALM/STORM). Specifically, in a biological sample incorporating a diarylethene compound, the ON (open-ring) molecules can be turned to OFF (close- ring) state by irradiation with different light, then a small number of molecules can be turned on by irradiation with UV light again for observation, and repetition of this process allows the position of the independent molecules to be detected and an image with higher resolution to be obtained.

EXAMPLES

[Example 1-1] Synthesis of Thiophene Compound

[0065] The reaction scheme is shown below.

[Formula 12]



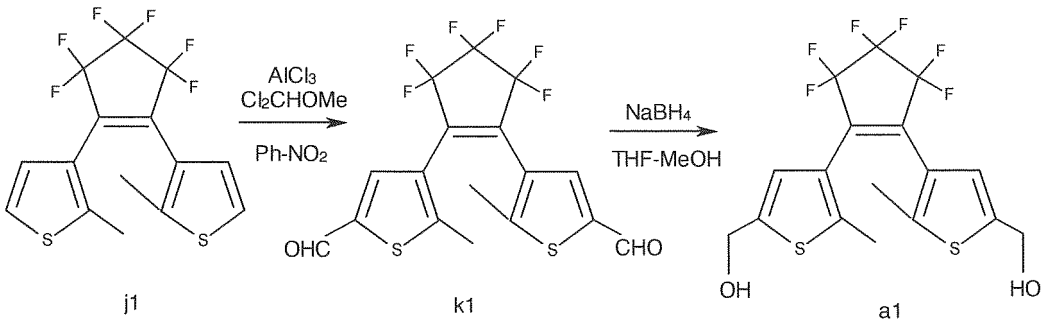
1) Synthesis of Acyl Halogenated Sugar

[0066] A compound (bromotetraacetoglucose) composed of glucopyranose having the hydroxyl group on the position-1 carbon atom substituted with Br, and having all other hydroxyl groups protected with acetyl groups, was prepared as an acyl halogenated sugar. Specifically, the compound was synthesized in the following manner. Pentaacetyl glucopyranose (TCI) was dissolved in an excessive amount of hydrogen bromide-acetic acid solution (hydrogen bromide: acetic acid=1:1 (mol rate)), then, it was sealed and reacted for a day and a night at room temperature to quantitatively obtain bromotetraacetoglucose.

2) Synthesis of Diols of Formula (a1)

[0067] The compound is a diol in which linking group U (methylene group) binds to position-5 of the thiophene ring. The diol was prepared by the following reaction.

[Formula 13]



The method of Non-Patent Document 5 was used to prepare a compound of formula (j1), then the compound was used to obtain a diformyl of formula (k1). $NaBH_4$ (51 mg, 2 eq.) was added to the THF-MeOH (3 m/3 mL) solution of the

diformyl (667 μmol) at 0°C in two separate instances, then the solution was agitated at 0°C for 4 hours. The reaction solution was diluted with ethyl acetate, then the organic layer was washed with water (3 times) and with saturated saline solution (once) in that sequence, and dried with sodium sulfuric acid. The drying agent was filtered out and the solvent was decompressed/removed, then the residue was refined by column chromatography (hexane: ethyl acetate=2:1) to obtain a diol of formula (a1).

3) Synthesis of Intermediate Represented by Formula (b1)

[0068] The diol of formula (a1) (69 mg, 0.16 mmol) and bromotetraacetoglucose (197 mg, 0.48 mmol) were dissolved in CH_2Cl_2 (3 mL), and 0.2 g of molecular sieve 4Å (by NACALAI TESQUE, INC.) was added to the mixture to be agitated for 1 hour at room temperature. Ag_2O (111 mg, 0.48 mmol) was further added under an argon airflow at room temperature with the light blocked, then the mixture was agitated for 24 hours. After the reaction ended, the un-dissolved matter was filtered out under reduced pressure, the filtrate was decompressed/concentrated, and the residue was separated/refined by silica gel column chromatography (hexane: ethyl acetate = 2:1 to 1:1) to obtain an intermediate represented by formula (b1) (96 mg, yield 52%).

[0069] The intermediate was analyzed using a mass analysis device (Model No. JMS-T100LC, by JEOL Ltd) and a peak of $[M+Na]^+$=1111 was obtained. The analysis was measured by the ESI positive mode, so the result included the target and Na (atomic weight 23) derived from the solvent or glass. Hence, the peak is a result of the target mass 1088, indicating that the obtained compound is a compound of formula (b1).

[0070] ESI-MS m/z: 1111 $[M + Na]^+$.
HR-ESI-MS m/z: 1111.21787 $[M + Na]^+$ (Calcd for $C_{45}H_{50}F_6NaO_{20}S_2$, 1111.21387).

4) Synthesis of the Compound of Formula (I-1) (Target Compound)

[0071] A compound represented by formula (b1) (38 mg, 0.03 mmol) and 2 mL of methanol were introduced into a three neck flask and agitated to form a homogenous solution. Potassium carbonate (13 mg, 0.3 mmol) was introduced into the flask, and a reaction was performed at room temperature for 15 hours. The reaction mixture was subjected to gel filtration/refinement by Bio-Gel P-2 Gel (by Bio-Rad) to obtain a compound of formula (I-1) in which 2 hydroxyl groups are protected by acetyl groups. The yield of the deprotection reaction was 56%.

5) Assessment of Water-Solubility

[0072] When an aqueous solution incorporating a small amount (50 μL) of methanol was prepared, and 2.5 mg of the compound of formula (I-1) was added to the solution, a reddish violet solution was obtained, indicating that the compound was dissolved. Likewise, when the compound of formula (I-1) was dissolved in water that does not contain methanol, a reddish violet solution was obtained, indicating that the compound was dissolved. In addition, the compound (I-1) was dissolved in a small amount of methanol, to which distilled water (4 mL) was added to prepare a 95% aqueous solution, and hence, an absorption spectrum of Fig. 1 (by Hitachi, using U-4100) was obtained. The spectrum of the open ring form is shown by dotted line 10. Irradiation with the UV light (313 nm) turned the solution purple, and a spectrum shown by solid line 20 was observed.

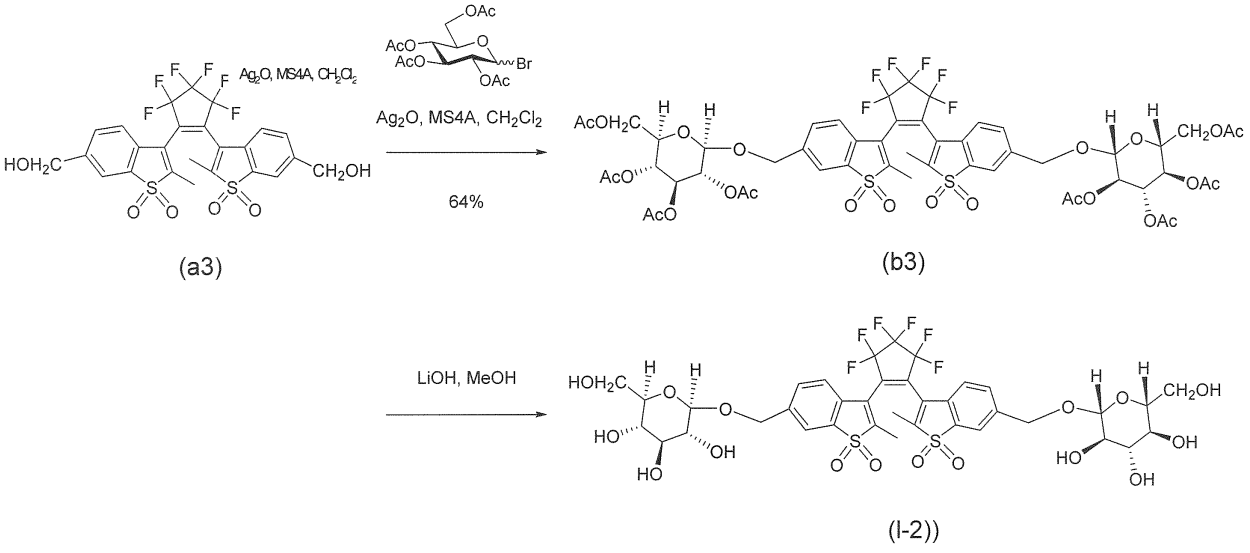
[Example 1-2] Synthesis of a Thiophene Compound

[0073] A compound of formula (I-1) was produced similarly to Example 1-1, except for using lithium hydroxide instead of potassium carbonate (5 mol equivalent against diaryl ethene). A compound of formula (I-1) having 2 hydroxyl groups protected by acetyl groups was obtained as a result. The obtained compound included 2 acetyl groups. The yield in the deprotection reaction was 56%.

[Example 2] Synthesis of Benzothiophene Sulfone

[0074] The reaction scheme is shown below.

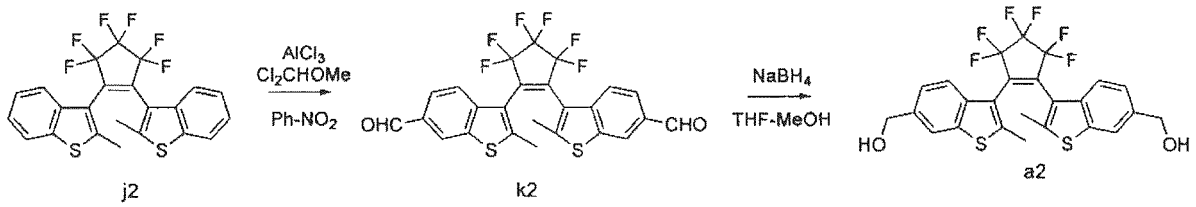
[Formula 14]



1) Synthesis of Diols of Formula (a2)

[0075] The compound is a diol including benzothiophene rings binding to linkage groups U (methylene group) at position-6. The diol was prepared by the following reaction.

[Formula 15]



[0076] A compound of formula (j2) prepared by the method of Non-Patent Document 6 was formylated to obtain a diformyl of formula (k2).

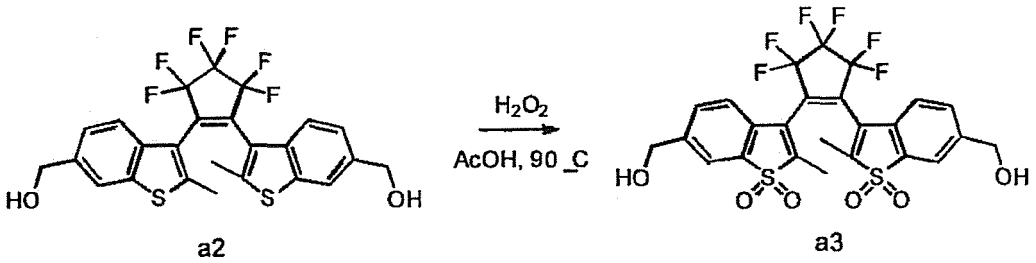
[0077] $NaBH_4$ (51 mg, 2 eq.) was added to the THF-MeOH (3 mL/3 mL) solution of the diformyl (350 mg, 667 μmol) at 0°C in two separate instances, then the solution was agitated at 0°C for 4 hours. The reaction solution was diluted with ethyl acetate, then the organic layer was washed with water (3 times) and with saturated saline solution (once) in that sequence, and dried with sodium sulfuric acid. A drying agent was filtered out and the solvent was decompressed/removed, and the residue was refined by column chromatography (hexane: ethyl acetate=2:1) to obtain a diol of formula (a2) (220 mg, 62% yield) as a pale red amorphous. The mass analysis result of the compound was as shown below.

[0078] ESI-MS m/z: 551 $[M + Na]^+$.
HR-ESI-MS m/z: 551.05427 $[M + Na]^+$ (Calcd for $C_{25}H_{18}F_6NaO_2S_2$, 551.05501).

2) Synthesis of Diols of Formula (a3)

[0079] The compound was prepared by the following reaction.

[Formula 16]



a2 a3

[0080] Acetic acid (2.5 mL) was added to the diol of a2 (50 mg, 95 μmol), and the mixture was heated to dissolve the diol. Hydrogen peroxide solution (35%, 370 μL) was added to the reaction solution and agitated at 90°C for 2 hours. After cooling, the reaction solution was diluted with ethyl acetate, then the organic layer was washed with water (3 times) and with saturated saline solution (once) in that sequence, and dried with sodium sulfuric acid. A drying agent was filtered out and the solvent was decompressed/removed, and the residue was refined by column chromatography (hexane: ethyl acetate=2:1 to 1:1) to obtain a diol (39 mg, 70% yield) of formula (a3) and a monoacetyl (6.9 mg, 12% yield) each as a pale yellow amorphous. The mass analysis result of the diol of formula (a3) was as shown below.

[0081] ESI-MS m/z: 615 $[M + Na]^+$.

HR-ESI-MS m/z: 615.03291 $[M + Na]^+$ (Calcd for $C_{25}H_{18}F_6NaO_6S_2$, 615.03467).

3) Synthesis of Intermediate Represented by Formula (b3)

[0082] The diol (14 mg, 0.024 mmol) of formula (a3) and bromotetraacetoglucose (97 mg, 0.24 mmol) were dissolved in CH_2Cl_2 (2 mL), and 0.1 g of molecular sieve 4Å was added to the mixture to be agitated at room temperature for 1 hour. Ag_2O (56 mg, 0.24 mmol) was further added under an argon airflow at room temperature with the light blocked, then the mixture was agitated for 24 hours. After the reaction ended, the un-dissolved matter was filtered out under reduced pressure, the filtrate was decompressed/concentrated, and the residue was separated/refined by silica gel column chromatography (hexane: ethyl acetate = 2:1 to 1:1) to obtain an intermediate represented by formula (b3) (16 mg, yield 64%) as a pale green amorphous.

[0083] The compound was subjected to mass analysis similarly to Example 1, and the peak was $[M+Na]^+$=1275. The peak comes from the target mass 1252, indicating the obtained compound is an intermediate represented by formula (b3).

[0084] ESI-MS m/z: 1275 $[M + Na]^+$.

HR-ESI-MS m/z: 1275.22742 $[M + Na]^+$ (Calcd for $C_{25}H_{18}F_6NaO_6S_2$,1275.22483).

4) Synthesis of Compound of Formula (I-2) (Target Compound)

[0085] The intermediate (10 mg, 0.008 mmol) represented by formula (b3) is dissolved in methanol (2 mL), to which lithium hydroxide (3 mg, 0.08 mmol) was added at room temperature, then the mixture was agitated for 24 hours. After the reaction ended, the reaction solution was decompressed/concentrated, and the residue was separated/refined with Bio-Gel P-2 (H_2O) to obtain a reaction mixture. When the reaction mixture was mass analyzed, the peak was 917. The peak is derived from the target compound mass 916, indicating that the obtained compound is the compound of formula (I-2).

[0086] ESI-MS m/z: 917 $[M + H]^+$.

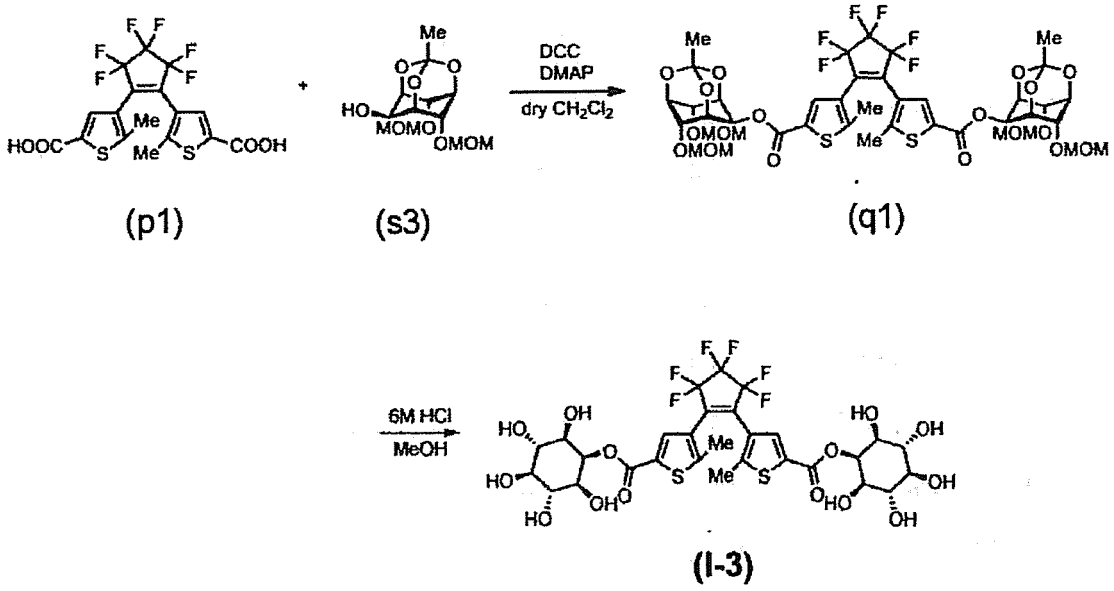
5) Analysis of Water Solubility

[0087] The water solubility of a compound of formula (I-2) was assessed similarly to Example 1, to check that the compound is water soluble. Specifically, the compound of (I-2) was dissolved in a small amount of methanol (0.2 mL), and distilled water (4 mL) was added to prepare a 95% aqueous solution, and an absorption spectrum of Fig. 2 (by Hitachi, using U-4100) was obtained as a result. The spectrum of the open ring form is shown by dotted line 10. Irradiation with a UV light (313 nm) turned the solution yellow, and a spectrum shown by solid line 20 was observed. In addition, the irradiation with the UV light made the compound fluorescent, and a spectrum of solid line 30 was obtained.

[Example 3] A benzothiophene Compound (Second Production Method)

[0088] The reaction scheme is shown below.

[Formula 17]



(p1) (s3) (q1)

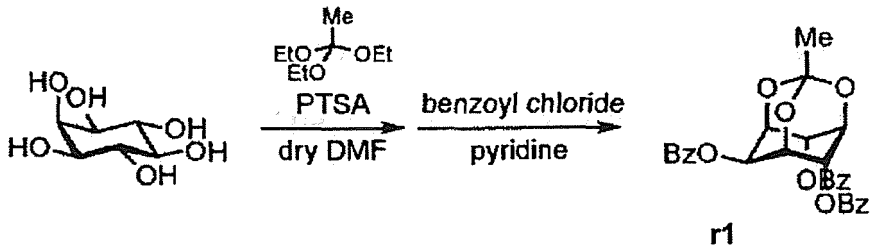
(I-3)

1) Synthesis of Protected Sugar

Synthesis of 2,4,6-Tri-O-benzoyl-Myo-Inositol 1,3,5-Orthoacetate (r1)

[0089]

[Formula 18]



r1

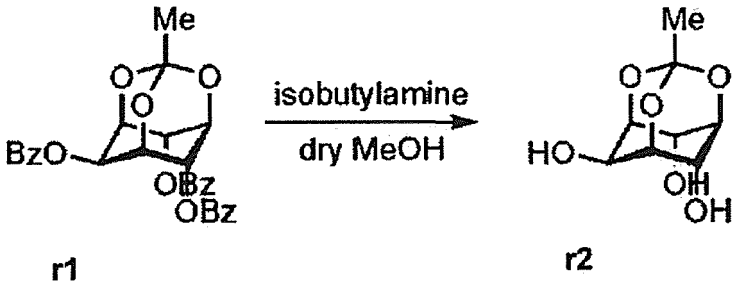
[0090] Myo-inositol (Tokyo Chemical Industry, 11.0 g, 61.1 mmol) and triethylorthoacetate (16.5 mL, 90.5 mmol) were added to dry DMF (80 mL). After reflux at 100°C for 30 minutes, p-toluenesulfonic acid monohydrade (Tokyo Chemical Industry, 1.14 g, 5.99 mmol) was added after dissolution in dry DMF (10 mL). Then, reflux of the content per se was performed at 100°C for 7.5 hours. The content temperature was readjusted to room temperature, trimethyl amine (Tokyo Chemical Industry, 4.0 mL, 28.9 mmol) was added, and the resulting material was agitated for 30 minutes. Further, benzene was added (10x2 mL), and the solvent was decompressed/removed. Then, pyridine (60 mL) was added. The content was cooled to 0°C, and benzoyl chloride (Tokyo Chemical Industry, 24.2 mL, 210 mmol) was dropped over a length of 1 hour. The content temperature was readjusted to room temperature, and the content was agitated for 16 hours. The content was recrystallized with methanol to produce a white solid compound r1 (21.2 g, 41.0 mmol, 67.1%). The results of the NMR (by JEOL Ltd., GSX400) and the mass analysis (Shimadzu Corporation, GCMS-QP2010) of the compound are as shown below.

[0091] ^{1}H NMR (400 MHz, CDC13): δ1.63 (s,3H), 4.68-4.70 (m, 2H), 4.91-4.94 (m, 1H), 5.65 (m. 1H), 5.81 (m, 4H), 7.17-7.21 (m, 1H), 7.46-7.51 (m, 4H), 7.60-7.64 (m, 1H), 7.85-7.87 (m, 4H), 8.16-8.19 (m, 2H)
MS (FAB) m/z = 516 [M]+

Synthesis of Myo-Inositol-1,3,5-Orthoacetate (r2)

[0092]

[Formula 19]



r1 r2

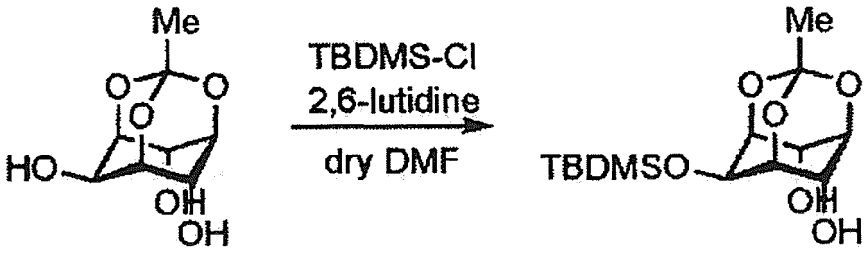
[0093] Under a nitrogen atmosphere, a compound of formula (r1) (18.0 g, 34.8 mmol), isobutylamine (Tokyo Chemical Industry, 14.0 mL, 49.9 mmol) were added to dry MeOH (60 mL) in the flask. Reflux of the content was performed at 65°C for 24 hours. The solvent was decompressed/removed, and diethyl ether was added to the solvent, then the mixture was cooled in an ice bath. The resulting precipitation was filtered out under reduced pressure, and a compound r2 (6.16 g, 30.2 mmol; 86.7%) was obtained as a white powder. The analysis result was as shown below.

[0094] ^{1}H NMR (400 MHz, CD_3OD): δ1.36 (s, 3H), 4.07-4.09 (m, 4H), 4.36-4.38 (m, 2H) MS (FAB) m/z = 204 [M+]

Synthesis of 2-O-Tert-Butyldimethylsilyl-Myo-Inositol-1,3,5-Orthoacetate (r3)

[0095]

[Formula 20]



r2 r3

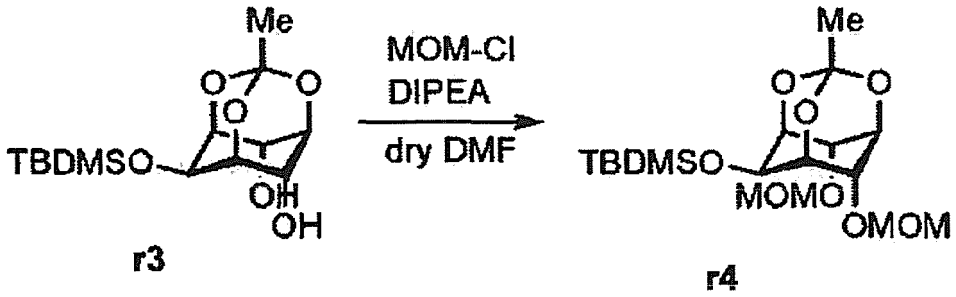
[0096] Under a nitrogen atmosphere, a compound of formula (r2) (3.26 g, 16.0 mmol), tert-butyldimethylchlorosilane (Tokyo Chemical Industry, 2.39 g, 15.9 mmol), 2,6-lutidine (Tokyo Chemical Industry, 5.0 mL, 42.9 mmol) were dissolved in the dry DMF (30 mL) in the flask. The content was agitated at room temperature for 36 hours. The solvent was decompressed/removed, and water (30 mL) was added. The solvent was cooled in an ice bath, and the resulting precipitate was filtered to obtain compound r3 (2.92 g, 9.17 mmol, 57.8%). The analysis result was as shown below.

[0097] ^{1}H NMR (400 MHz, $CDCl_3$); δ 0.15 (s, 6H), 0.95 (s, 9H), 1.45 (s, 3H), 4.14-4.16 (m, 2H), 4.18-4.20 (m,1H), 4.21-4.23 (m, 1H), 4.52-4.54 (m, 2H)
MS (FAB) m/z = 319 [M+1]+

Synthesis of 2-O-Tert-Butyldimethylsilyl-4,6-Bis(O-Methoxymethyl)-Myo-Inositol-1,3,5-Orthoacetate (r4)

[0098]

[Formula 21]



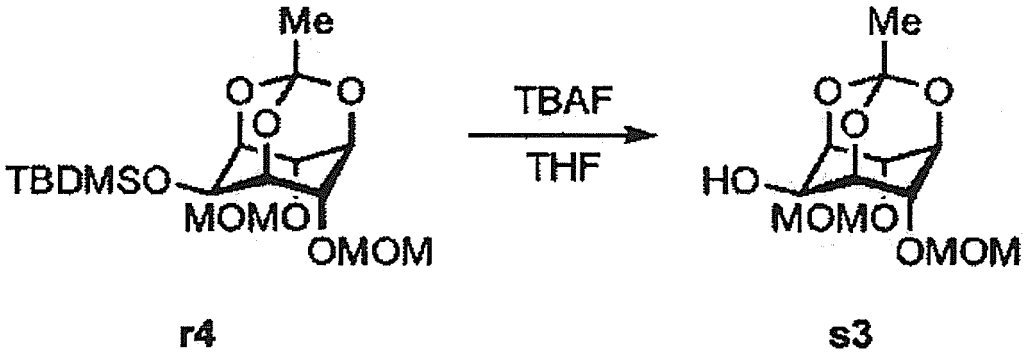
[0099] A compound of formula (r3) (1.77 g, 5.56 mmol) was dissolved in the dry DMF (30 mL) in a flask under a nitrogen atmosphere. N,N-Diisopropylethylamine (Tokyo Chemical Industry, 4.0 mL, 40.7 mmol) was added and methoxymethyl chloride (Tokyo Chemical Industry, 2.5 mL, 33.2 mmol) was dropped thereto. Reflux of the content was performed at 65°C for 36 hours. The solvent was decompressed/removed, and extraction was performed using ethyl acetate. The resulting product was dried with magnesium sulfate, then a residue was refined by silica column chromatography (eluent; chloroform: methanol=8:1) to obtain compound r4 (1.69 g, 4.16 mmol, 74.8%). The analysis result was as shown below.

[0100] ^{1}H NMR (400 MHz, $CDCl_3$); δ0.13 (s, 6H), 0.94 (s, 9H), 1.45 (s, 3H), 3.34 (s, 6H), 4.11-4.13 (m, 2H), 4.16-4.17 (t, J = 2.0 Hz, 1H), 4.27-4.29 (m, 1H), 4.35-4.37 (m, 2H), 4.40-4.42 (m, 4H)
MS (FAB) m/z = 407 [M+1]+

Synthesis of 4,6-Bis(O-Methoxymethyl)-Myo-Inositol-1,3,5-Orthoacetate (s3)

[0101]

[Formula 22]



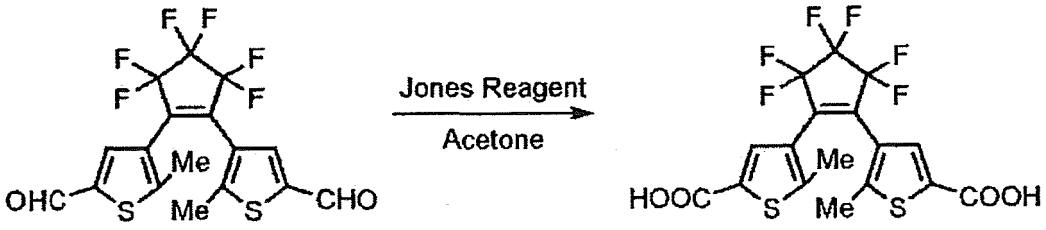
[0102] The compound of formula (r4) (1.59 g, 3.91 mmol) was dissolved in THF (15 mL) in the flask. Then, 1.0 mol/L of tetrabutylammonium fluoride (Tokyo Chemical Industry)-THF solution (5.1 mL, 5.1 mmol) was added and the mixture was agitated for 16 hours. The reaction was terminated with water (10 mL), then extraction was performed using diethylether, and drying was performed using magnesium sulfate. A residue was refined by silica gel column chromatography (eluent; hexane: ethyl acetate=6:1 to 4:1) to obtain compound s3 (0.82 g, 2.81 mmol, 71.8%). The analysis result was as shown below.

[0103] ^{1}H NMR (400 MHz, $CDCl_3$); δ 1.45 (s, 3H), 2.99 (d, J = 12 Hz, 1H), 3.39 (s, 6H), 4.01-4.05 (m, 1H), 4.21-4.23 (m, 2H), 4.26-4.29 (m, 1H), 4.43 (t, J = 3.8 Hz, 2H), 4.67-4.74 (m, 4H)
MS (FAB) m/z = 293 [M+1]+

2) Synthesis of Dicarboxylic Acids of Formula (p1)

[0104] Diformyls of formula (k1) were subjected to the following process to obtain dicarboxylic acids of formula (p1).

[Formula 23]



k1 p1

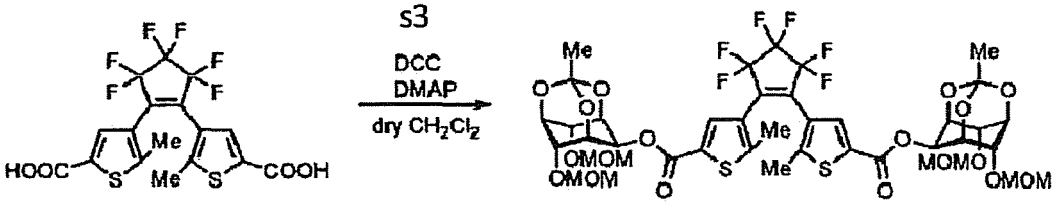
[0105] CrO_3 (3.19 g, 31.9 mmol) was dissolved in water (4.5 mL), and the solution was cooled with an ice bath, while concentrated sulfuric acid (3.0 mL) and water (9.0 mL) were added to prepare the Jones reagent. Then, the compound of formula (k1) (3.22 g, 7.59 mmol) was dissolved in acetone (80 mL) in the flask. The Jones reagent was dropped slowly in the flask, and the content of the flask was agitated for 17 hours. The reaction was terminated using 2-propanole (20 mL). Extraction was performed using diethylether, and drying was performed using magnesium sulfate. The solvent was decompressed/removed, and recrystallization was performed using ethyl acetate/hexane to obtain p1 (3.07 g, 6.73 mmol, 86.7%) as a white powder. The analysis result was as shown below.

[0106] 1H NMR (400 MHz, CD3OD): 1.99 (s, 3H, Me), 7.72 (s, 1H, thienyl)
MS (EI) m/z = 456 [M]+

3) Synthesis of Intermediate Represented by Formula (q1)

[0107]

[Formula 24]



p1 q1

[0108] Under a nitrogen atmosphere, the dicarboxylic acid of formula (p1) (320 mg, 0.701 mmol), N,N'-dicyclohexyl-carbodiimide (0.415 mg, 2.01 mmol), 4-dimethylaminopyridine (30 mg, 0.246 mmol) were dissolved in dry CH_2Cl_2 (6mL), and the mixture was agitated at room temperature for 30 minutes.

[0109] Then, the protected sugar of formula (s3) (480 mg, 1.64 mmol) was dissolved in dry CH_2Cl_2 (2 mL) to be added to the above solution, and agitated at room temperature over night. The generated solid was filtered under reduced pressure and washed with CH_2Cl_2. The solvent was decompressed/removed, and a residue was refined by silica gel column chromatography (eluent; dichloromethane: ethyl acetate=4:1) to obtain a pale yellow powder of an intermediate of formula (q1) (405 mg, 0.403 mmol, 58% yield). The results of NMR (by JEOL Ltd., GSX400) and mass analysis (Shimadzu Corporation, GCMS-QP2010) were as shown below. The analysis result was as shown below.

[0110] ^1H NMR (400 MHz, $CDCl_3$): d 1.48 (s, 3H), 2.01 (s, 3H), 3.43 (s, 6H), 4.33 (sep, J= 1.6 Hz, 1H), 4.42-4.43 (m, 2H), 4.46 (t, J = 3.8 Hz, 2H), 4.71-4.78 (m, 4H), 5.43 (t, J= 1.8 Hz, 1H), 7.83 (s, 1H)
MS (FAB) m/z = 1004 [M^+]

4) Synthesis of Compound of Formula (I-3) (Target Compound)

[0111] The intermediate represented by formula (q1) (290 mg, 0.289 mmol) was dissolved in methanol (5 mL). To the resulting solution, hydrochloric acid of 6 mol/L (25 mL) was added, and reflux of the solution was performed at 55°C for 6 hours. Then, hydrogen chloride was trapped with sodium carbonate, while the solvent was decompressed/removed. The residue was refined by reversed-phase silica gel column chromatography (eluent; methanol: water=4:1) to obtain the compound of formula (I-3) (210 mg, 0.269 mmol, 93% yield). The analysis result was as shown below.

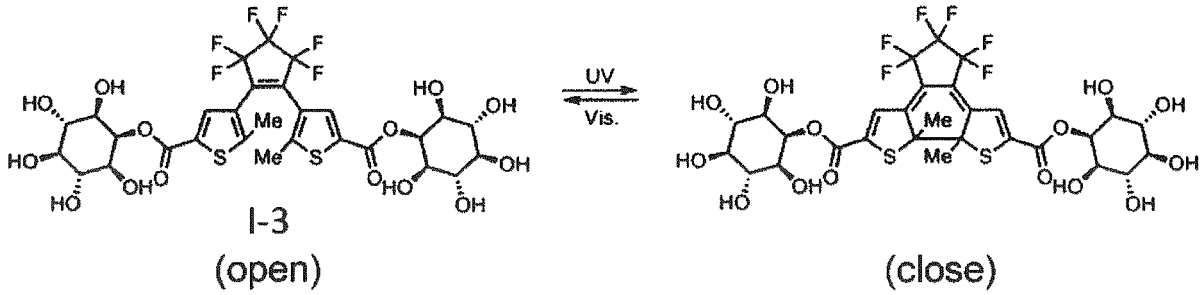
[0112] ^{1}H NMR (400 MHz, CD_3OD): d 2.07 (s, 3H), 3.60-3.62 (m, 5H), 5.56 (s, 1H), 7.73 (s, 1H)
MS (FAB) m/z = 780$[M]^+$

5) Analysis of Water Solubility

[0113] The water solubility of a compound of formula (I-3) was assessed in a similar manner as Example 1 to confirm that the compound is water soluble.

[0114] The absorption spectrum (using U-4100 of Hitachi) of the aqueous solution thus obtained is shown in Fig. 3. Curve 10 is a spectrum of the compound (open ring form) of formula (I-3), and the maximum absorption wave length was 254 nm. Then, an aqueous solution of the compound of formula (I-3) was irradiated with light of 254 nm to obtain a photostationary state (PSS), in which the ring closing reaction has ended. The spectrum at this state is shown as curve 20. The maximum absorption wavelength of the closed ring form was 595 nm. The spectrum returned to the original spectrum upon irradiation with visible light longer than 600 nm indicating the reversible photochromism (the following scheme).

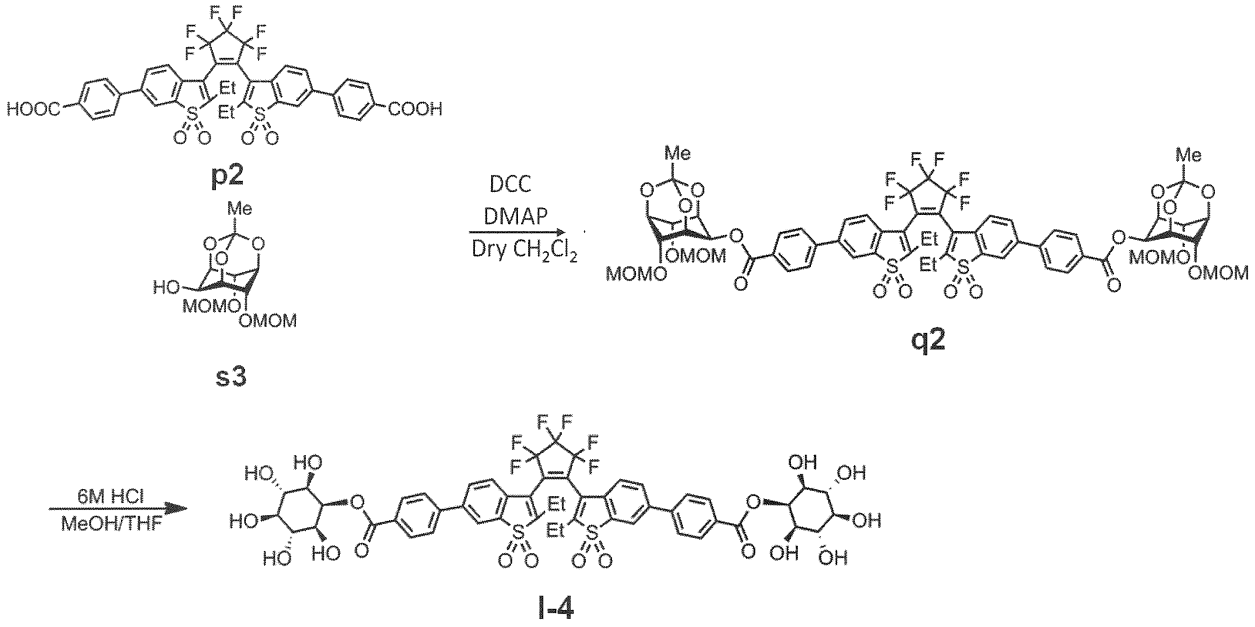
[Formula 25]



[Example 4] Benzothiophene Sulfone Compound

[0115] The reaction scheme is shown below.

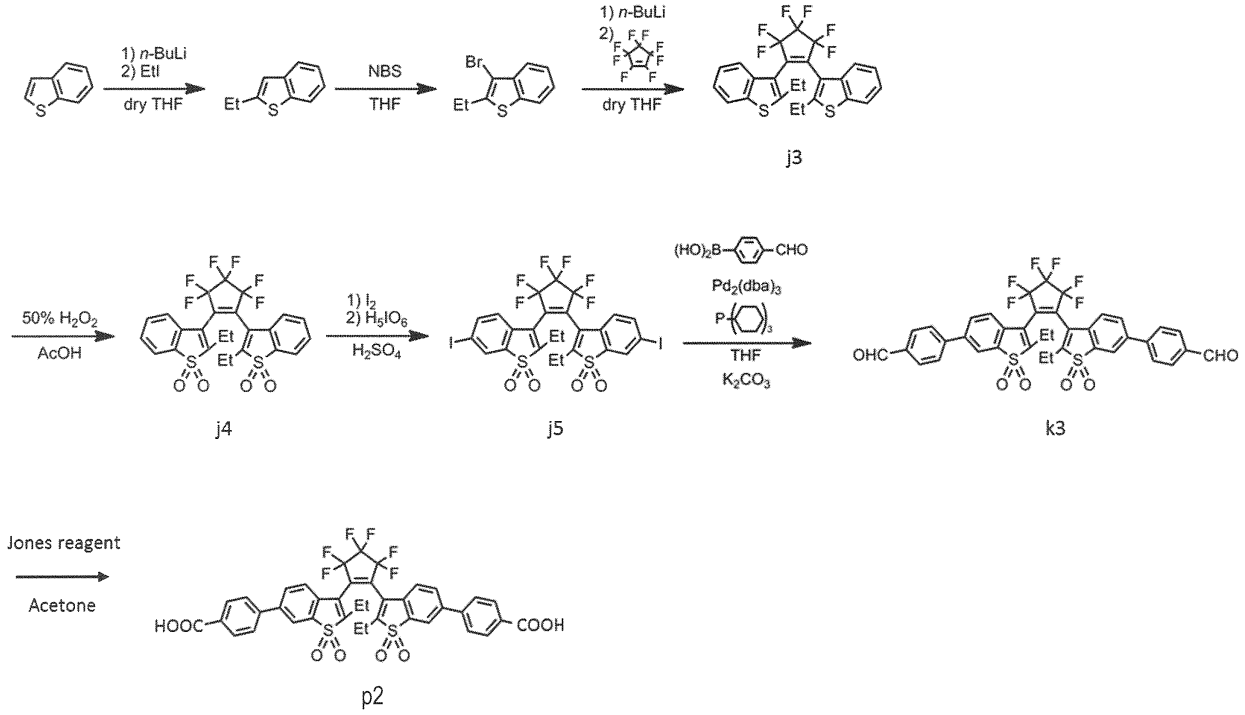
[Formula 26]



1) Synthesis of Dicarboxylic Acids of Formula (p2)

[0116] The reaction scheme is shown below.

[Formula 27]



[0117] The compound of formula (j3) was synthesized according to Non-Patent Document 6. The compound of formula (j4) was synthesized according to the synthesis method in 2) of Example 2. The compound of formula (j5) was synthesized by applying a common method using iodine and H_5IO_6 and introducing iodine in the compound of formula (j4)

[0118] The compound of formula (j5) (450 mg, 0.450 mmol) and 4-formylphenylboronic acid (199 mg, 1.33 mmol) were dissolved in THF (10 mL).

Tris(dibenzylideneacetone)dipalladium (0) (95 mg, 0.104 mmol), potassium carbonate solution (10 mL), and an 18% toluene solution of tricyclohexylphosphine (0.1 mL) were added to the solution, then the resulting solution was agitated at room temperature for 20 minutes. The reaction product was treated with hydrochloric acid, then extraction was performed using chloroform. The extract was dried with magnesium sulfate, then the solvent was removed, and a residue was refined by silica gel column chromatography (eluent: hexane/ethyl acetate=4/1, 2/1) to obtain the compound of formula (k3). The yield amount was 353 mg (0.459 mmol), and the yield rate was 82.9%. The analysis result was as shown below.

MS (EI) m/z = 768 [M^+]

[0119] The compound of formula (k3) (200 mg, 0.260 mmol) was dissolved in acetone (10 mL) and an adjusted Jones reagent (0.6 mL, 1.17 mmol) was slowly dropped in the solution, then the solution was agitated overnight. The reaction was terminated using 2-propanol (2 mL), and the solvent was decompressed/removed. Extraction from the reaction product was performed using ethyl acetate, and the extract was dried with magnesium sulfate, then, the solvent was removed. Recrystallization was performed using ethyl acetate and hexane to obtain a compound of formula (p2). The yield amount was 122 mg (0.152 mmol) and the yield rate was 73.3%. The analysis result was as shown below.

MS (ESI) m/z = 823.0865 [M+Na]$^+$

2) Synthesis of Intermediate of Formula (q2)

[0120] The compound of formula (p2) (366 mg, 0.457 mmol), N,N-dicyclohexylcarbodiimide (283 mg, 1.37 mmol), 4-dimethylaminopyridine (19 mg, 0.152 mmol) were dissolved in dry dichloromethane (DCM) (12 mL) and agitated at room temperature for 30 minutes. A compound of formula (s3) (401 mg, 1.37 mmol), prepared in the above manner, was dissolved in dry dichloromethane (1 mL) to prepare a solution, then, the solution was added to a mixture containing the compound of formula (p2) and the resulting mixture was agitated overnight. The precipitation was removed by filtration under reduced pressure, and the solvent was decompressed/removed. A residue was refined by silica gel column chromatography (dichloromethane: ethyl acetate=4:1) to obtain a compound of formula (q2). The yield amount was 65 mg (0.048 mmol), and the yield rate was 11%. The analysis result was as shown below.

MS (ESI) m/z = 1371.2971 [M+Na]$^+$

3) Synthesis of Compound of Formula (I-4) (Target Compound)

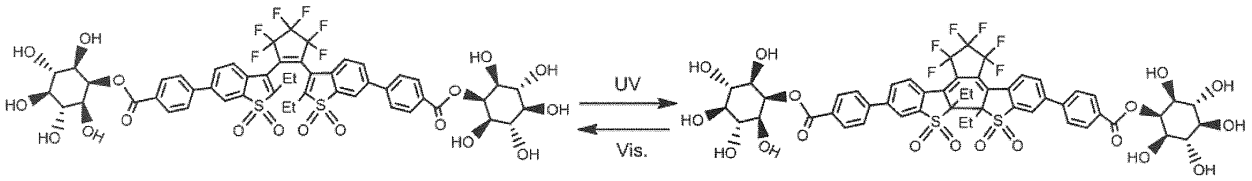
[0121] The compound of formula (q2) (50 mg, 0.037 mmol) was dissolved in THF (1 mL), to which methanol (1 mL), and HCl of 6M (5 mL) were added. After 6 hours of reflux at 60°C, toluene (10 mL) was added, and the solvent was decompressed/removed. A residue was refined by reverse-phase column chromatography (methanol: water=4:1) to obtain the target compound. The analysis result was as shown below.
MS (ESI) m/z = 1147.1922 $[M+Na]^+$

4) Analysis

[0122] About 0.5 mg of the given compound was dissolved in each of 0.5 mL of water/methanol (weight rate of 90/10) and 0.5 mL of only methanol to prepare a solution. For convenience, the former will be referred to as an aqueous solution, and the latter will be referred to as a methanol solution. The absorption spectrum of the solutions are shown in Figs. 4, 5. Curve 10 is a spectrum of the compound of formula (I-4) (open ring form). In the methanol solution, the maximum absorption wavelength is 450 nm, and the molar absorption coefficient was 39000 $M^{-1}cm^{-1}$. The absorption disappeared when irradiated with visible light, and the solution returned to a colorless state. Curve 20 is a spectrum of the closed ring form. The closed ring form showed a light green fluorescence (curve 30), the fluorescence maximum was observed at 520 nm, and the fluorescent quantum yield was 0.71. Further, the fluorescence disappeared when the compound returned to the open ring form. It was thus shown that the compound of formula (I-4) shows reversible photochromism and switching of fluorescence in methanol.

[0123] In the aqueous solution, the maximum absorption wavelength of the open ring form was 458 nm, and the molar absorption coefficient was 36000 $M^{-1}cm^{-1}$. The absorption disappeared when irradiated with visible light, and the solution returned to a colorless state. The closed ring form showed a yellow fluorescence (curve 30), the maximum luminescence was observed at 540 nm, and the fluorescent quantum yield was 0.44. Further, the fluorescence disappeared when the compound returned to the open ring form. It was thus shown that the compound of formula (I-4) shows reversible photochromism and switching of fluorescence in a mixed water/methanol (weight ratio of 90/10) solvent.

[Formula 28]



[Example 5]

[0124] About 0.5 mg of diarylethene of formula (I-4) was dissolved in 0.5 mL of methanol, to which water was added to prepare a water/methanol (weight ratio of 5/1) mixture. The solution was injected in the 4-cell stage embryo of a Xenopus. The state immediately after injection is shown in Fig. 6(a). The black spot at the upper left blastomere is the injection site. After injection, the cell was left untouched for about an hour to allow cell division (32-cell stage). The cells were irradiated with a UV light of 470 to 495 nm wavelength. Then, the cells were checked to see if there were any fluorescence, and fluorescence was confirmed around the injection site (Fig. 6 (b)).

[Example 6]

[0125] The solution prepared in Example 5 was placed on a 10 μm slice of tail-bud embryo head of a Xenopus and left untouched at room temperature for 30 minutes. Then, the tail-bud embryo head was washed with 10% methanol aqueous solution, and irradiated at a wavelength of 470-495 nm. Observation under bright field is shown in Fig. 7(a). The wavelength of 515 to 550 nm was detected under the dark field, but almost no light emission was seen as shown in Fig. 7(b). The subject was then irradiated with UV ray having a wavelength of 360 to 370 nm for 30 seconds, after which a wavelength of 515 to 550 nm was detected again (Fig. 7(c)). As shown in Fig. 7(c), the fluorescent signal was observed particularly on the outer layer of the epidermis of the embryo.

REFERENCE SIGNS LIST

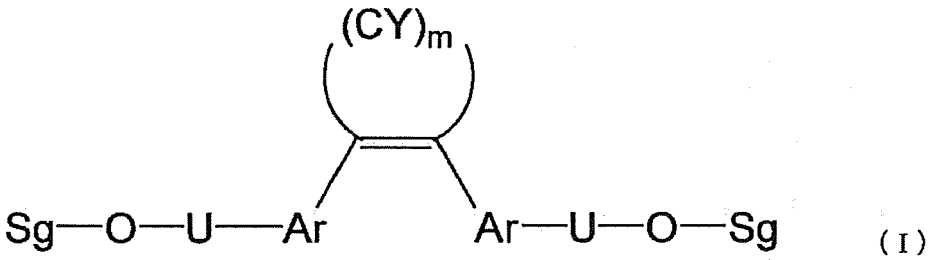
[0126]

10 Spectrum of open ring form
20 Spectrum of close ring form
30 Fluorescent spectrum

Claims

1. A diarylethene compound represented by formula (I):

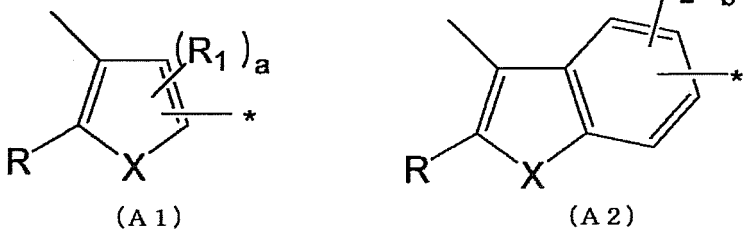
[Formula 1]



(I)

wherein, Sg is a monovalent sugar-type residue consisting of a sugar-type compound (in which some of hydroxyl groups may be protected) selected from a group consisting of a six-membered ring sugar, a five-membered ring sugar, cyclitol and oligosaccharides containing a six-membered ring sugar, a five-membered ring sugar, or cyclitol and excluding a hydroxyl group;
U is $-(CH_2)n-$, $-CH_2-U'-$, or $-C(=O)-$ (wherein, n is an integer of 1 to 5, U' is a C1-C10 alkyl group binding to Ar);
Ar is a group represented by formula (A1) or (A2);

[Formula 2]



wherein,

X is S, SO_2, NR_3 (R_3 is a C1-C3 alkyl group) or O,
R is C1-C4 alkyl group,
R_1 and R_2 are independently a C1-C3 alkyl group,
a is 0 or 1, b is an integer of 0-3, and
* represents a bond with U;
Y is a hydrogen atom or a halogen atom; and
m is an integer of 5-7.

2. The compound according to Claim 1, wherein the Sg is a monovalent sugar-type residue of pyranose excluding a

hydroxyl group.

3. The compound according to either Claim 1 or 2, wherein the Sg is a monovalent sugar-type residue of pyranose excluding a hydroxyl group on a position-1 carbon.

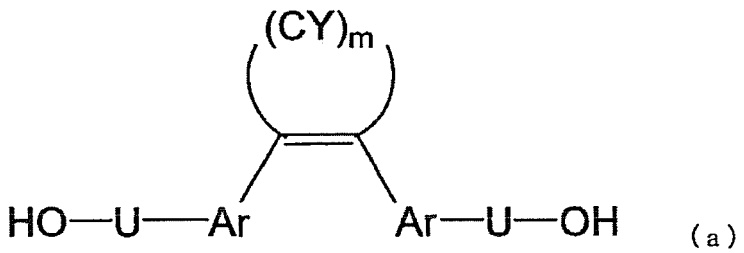
4. The compound according to either Claim 1 or 2, wherein the Sg is a monovalent sugar-type residue of cyclitol excluding a hydroxyl group.

5. The compound according to any one of Claims 1 to 4, wherein the X is S or SO_2.

6. A method for producing a diarlyethene compound according to any one of Claims 1 to 5, comprising:

(1) a step of preparing a halogenated sugar derivative derived from a sugar-type compound selected from a group consisting of a six-membered ring sugar, a five-membered ring sugar, cyclitol and oligosaccharides containing a six-membered ring sugar, a five-membered ring sugar, or cyclitol, and having 1 hydroxyl group substituted with a halogen atom, and all other hydroxyl groups protected by protection groups;
(2) an etherification step of reacting the halogenated sugar derivative with the compound represented by formula (a) to generate a compound represented by formula (b)

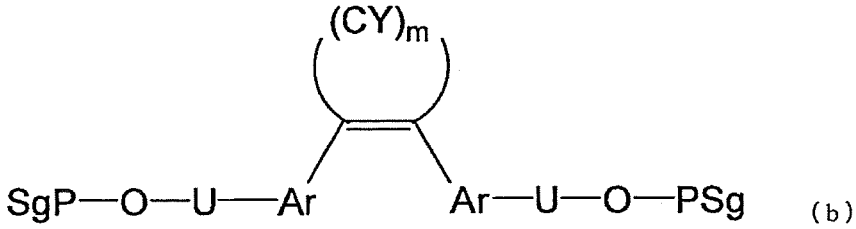
[Formula 3]



(a)

wherein, U, Ar, Y and m are as defined above;

[Formula 4]



(b)

wherein, U, Ar, Y and m are as defined above, and PSg shows a group in which all hydroxyl groups of the Sg are protected; and
(3) a deprotection step of removing a protection group of the compound represented by formula (b).

7. The method according to Claim 6, wherein the step (1) is performed under a presence of Ag_2O.

8. The method according to either Claim 6 or 7, wherein the halogen atom in the halogenated sugar derivative is bromine atom.

9. The method according to any of Claims 6 to 8, wherein a protection group in the halogenated sugar derivative is an acyl group.

Figure 1

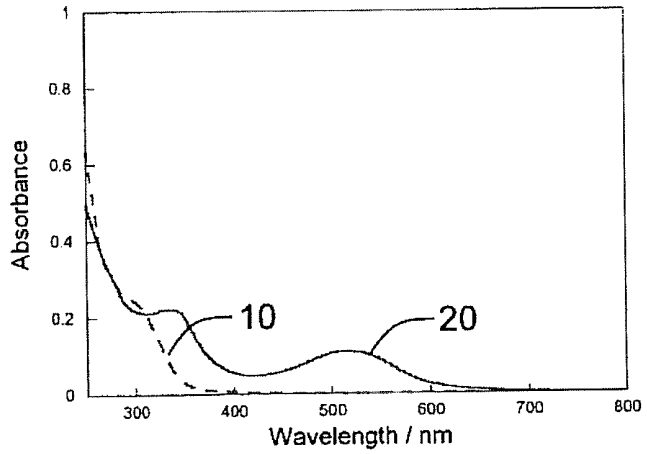


Figure 2

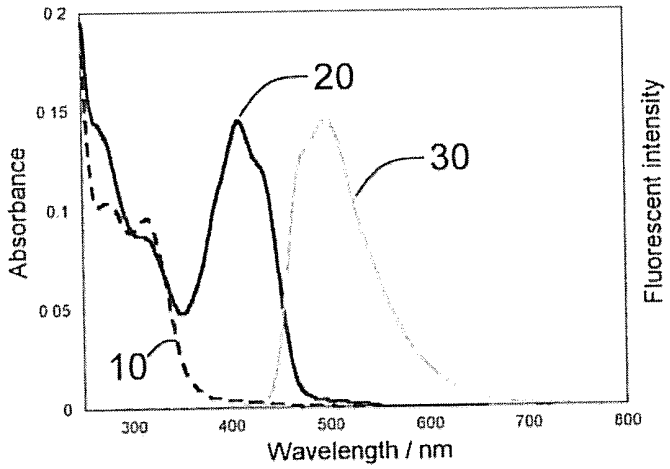


Figure 3

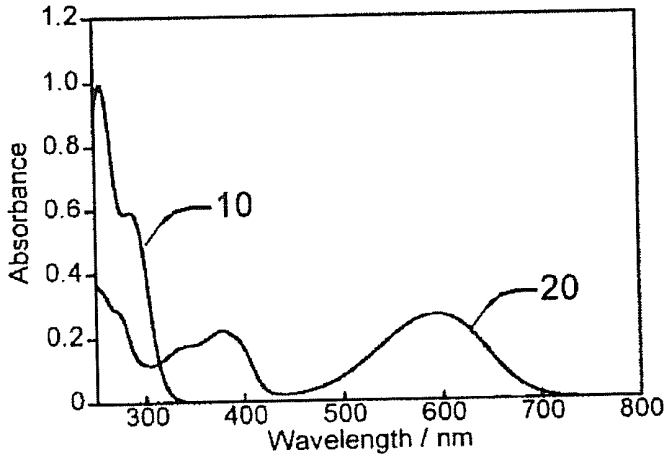


Figure 4

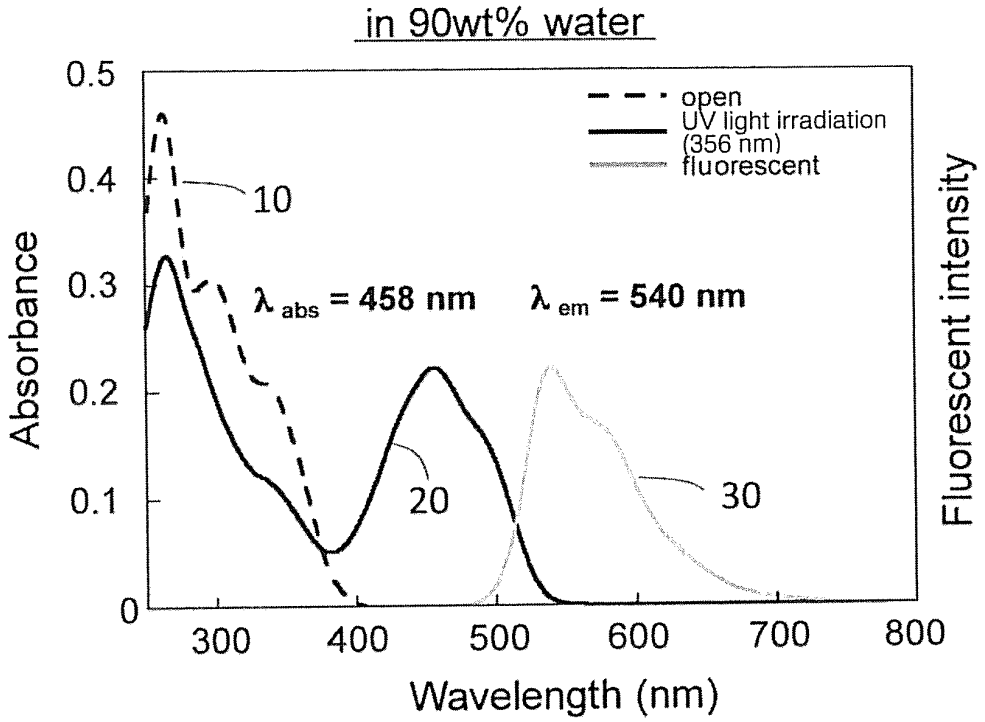


Figure 5

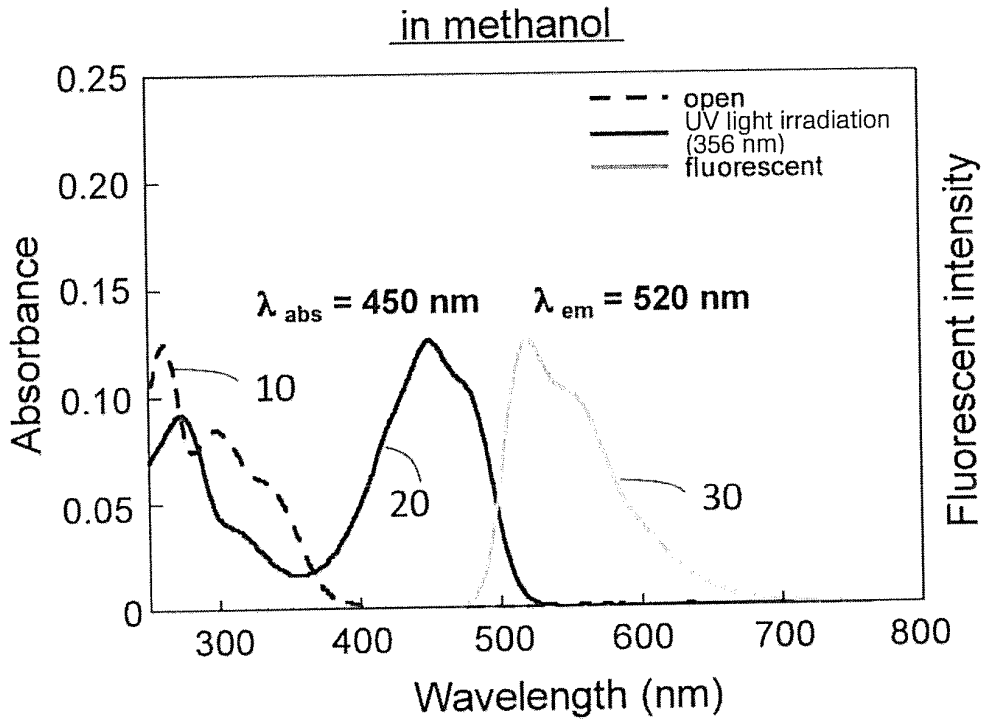


Figure 6

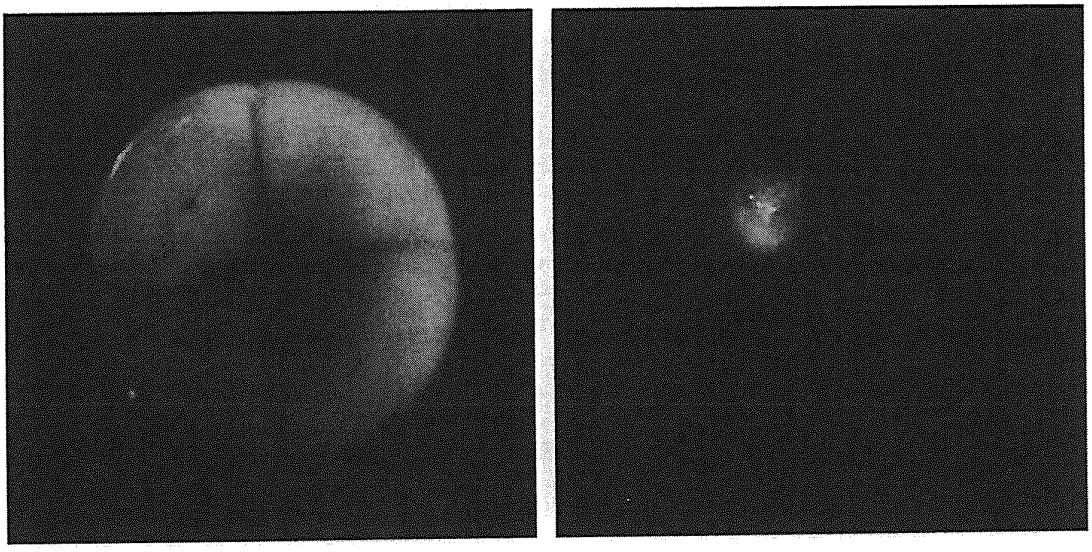
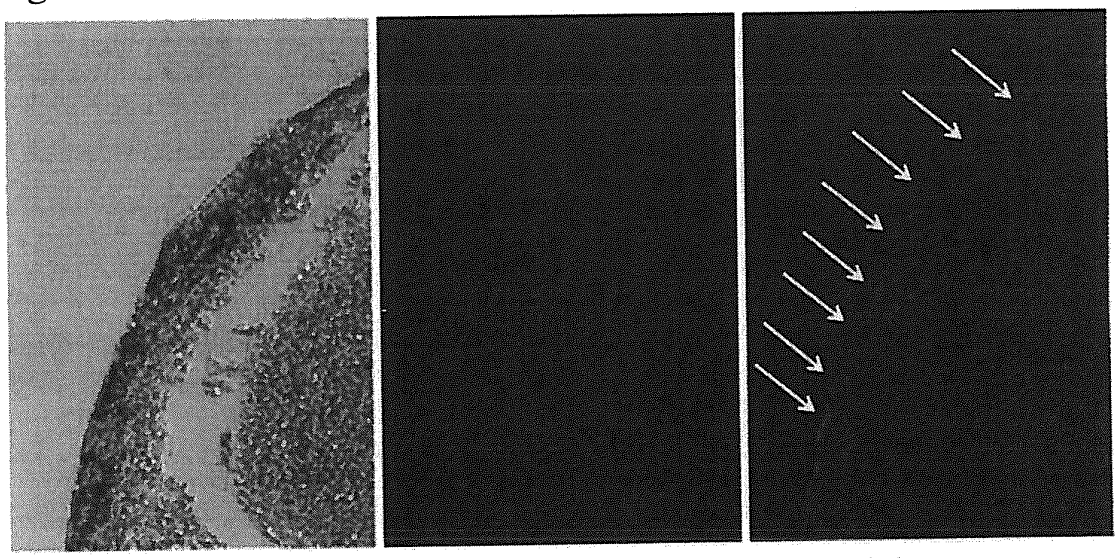


Figure 7



INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2013/074052

A. CLASSIFICATION OF SUBJECT MATTER
C07H15/26(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07H15/26

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Jitsuyo Shinan Koho 1922-1996 Jitsuyo Shinan Toroku Koho 1996-2013
Kokai Jitsuyo Shinan Koho 1971-2013 Toroku Jitsuyo Shinan Koho 1994-2013

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAplus/REGISTRY(STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	POLYAKOVA, S. M. et al., Synthesis of photochromic compounds for aqueous solutions and focusable light, Eur J Org Chem. 2011, v.2011, p.3301-3312, entire text	1-9
A	AYT, A. et al., Masking photochromic films for nanolithography technology, Phys Status Solidi C. 2011, v.8, p.2866-2869, entire text	1-9
A	COHEN, N. et al., Synthesis and characterization of light-driven dithienylcyclopentene switches with axial chirality, J Org Chem. 2011, v.76, p.7148-7156, entire text	1-9

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 November, 2013 (13.11.13)	26 November, 2013 (26.11.13)
Name and mailing address of the ISA/ Japanese Patent Office Facsimile No.	Authorized officer Telephone No.

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2013/074052

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2006/080647 A1 (SAMSUNG ELECTRONICS CO., LTD.), 03 August 2006 (03.08.2006), entire text & US 2006/0079653 A1 & CN 101027308 A & KR 10-2006-0051627 A	1-9
A	JP 2005-082507 A (Mitsubishi Chemical Corp.), 31 March 2005 (31.03.2005), entire text (Family: none)	1-9
A	KAWAI, S. H., Photochromic bis(monoaza-crown ether)s. Alkali-metal cation complexing properties of novel diarylethenes, Tetrahedron Lett. 1998, v.39, p.4445-4448, entire text	1-9

Form PCT/ISA/210 (continuation of second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2013/074052

Subject to be covered by this search:

Since claims 1-9 of the present application are not clearly set forth, the technical range of the inventions set forth in said claims cannot be objectively and clearly understood. In addition to this, it is also not considered that the inventions of claims 1-9 are set forth with substantiality in the description, and the inventions are lack in clarity and full support by the description within the meaning of PCT Article 5 and Article 6 respectively, and therefore, a full and meaningful prior-art search cannot be carried out.

Therefore, with respect to the invention in claims 1-9 of this application, a search report was made only on the part disclosed in and supported by the description, that is, the compound in which the cyclic ethene moiety containing the group "(CY)m" is a "five-membered ring" (namely, m is an integer of 3) and in which the remaining one substituent bonded to each carbon atom "C" contained in the "(CY)m" is "F (fluorine atom)".

Form PCT/ISA/210 (extra sheet) (July 2009)

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- JP 2005325087 A **[0006]**

Non-patent literature cited in the description

- **M. IRIE et al.** *Nature,* 2002, vol. 420, 759 **[0007]**
- **K. H. JONES ; J. A. SENFT.** *J. Histochem. Cytochem.,* 1985, vol. 33, 77 **[0007]**
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- **T. YAMAGUCHI et al.** *J. Photochem. Photobio. A,* 2006, vol. 178, 162 **[0007]**