Abstract: The present invention provides new intermediate compounds enabling the preparation of N-meso substituted cyanine, merocyanine or oxonole dyes wherein the N-meso substituent comprises electron withdrawing groups and wherein such N-meso substituents are introduced at the intermediate level. These intermediates enable the formation of dyes having in the meso-position N-substituents comprising electron withdrawing groups without the need for further derivatization of the meso-substituent at the dye level.
INTERMEDIATE COMPOUNDS FOR THE PREPARATION OF MESO-SUBSTITUTED CYANINE, MEROCYANINE AND OXONOLE DYES

[DESCRIPTION]

FIELD OF THE INVENTION

The present invention relates to new intermediate compounds according to Formula I. The invention relates also to a method of preparing cyanine, merocyanine or oxonole dyes from the new intermediate compounds.

BACKGROUND OF THE INVENTION

Cyanine, merocyanine or oxonole dyes are well known in the art. They are for example widely used in various imaging systems, in recording media such as optical discs or in diagnostic tools. For more information about the application of these dyes, see for example "COLOR CHEMISTRY: synthesis, properties and applications of organic dyes and pigments", Heinrich Zollinger, VHCA & Wiley-VCH, third revised edition 2003. Cyanine dyes are for example also used as infrared (IR) radiation absorbing dyes (IR-dyes) in lithographic printing plate precursors. These IR-dyes absorb IR radiation, used to imagewise expose the lithographic printing plate precursors, thereby triggering an imaging mechanism of the lithographic printing plate precursor, e.g. polymerization, coalescence of thermoplastic particles, solubilization or msolubilization, etc.

The preparation of cyanine dyes having a chloride atom as meso-substituent, for example according to the following formula wherein R represents a substituent and X^- renders the dye neutral, is well known in the art.
For example in WO2002/24815 the following reaction is disclosed to prepare such a meso-chlor cyanine dye.

It may however be advantageous to introduce other substituents than chloride on the meso-position of a cyanine dye, for example to change the absorption characteristics, to improve the thermal or photostability, to change the solubility or to adjust the hydrophobicity/hydrophilicity of the cyanine dye.

Often, to prepare cyanine dyes with other meso-substituents than chloride, the corresponding meso-Cl cyanine dye is first prepared as
intermediate dye, followed by an exchange of the chloride by the other substituent.

For example in WO2002/24815 cyanine dyes having as meso-substituent -O-Ar, -S-Ar, -NH-Ar or -NR-Ar, wherein Ar represents an aryl group and R an alkyl group, are prepared from the corresponding meso-Cl cyanine dye.

EP-A 1 736 312 and WO2006/136543 disclose IR-dyes enabling the formation of a visible printout image upon imagewise exposure of lithographic printing plate precursors, comprising those IR-dyes, to IR radiation. The formation of a visible printout image is the result of a chemical transformation of specific substituents, preferably on the meso-position of the cyanine dyes, upon exposure to IR-radiation. Again, these IR-dyes are all prepared by first preparing the corresponding meso-Cl IR-dye, followed by an exchange of the chloride with one of the specific substituents, either through a single step or a multistep reaction sequence.

In WO2004/052995, an intermediate product according to the following formula,

![Chemical Structure](image)

wherein L is for example a 5- or 6-membered ring and \(X^-\) renders the intermediate neutral, is used to obtain in a "one pot process" cyanine dyes having as meso-substituent -S-Ar; -Se-Ar; -O-Ar; -NR'-Ar; -SO\(_2\)-Ar or -(N-heterocycle), wherein Ar represents an aryl group and R' represents a hydrogen or an alkyl group. However, during this "one pot process" the corresponding meso-Cl cyanine dye is also formed first in situ, whereupon the chloride is replaced by the above mentioned substituents.

Another disadvantage of first synthesizing the meso-Cl dye is the fact that at least one additional reaction step is necessary and moreover, that the exchange of the chloride by the required substituent may be cumbersome, e.g. resulting in unwanted side reactions and/or intermediate products, depending on the nature of the required substituent and the other structural parts of the cyanine dye. An example of unwanted side-reactions that might occur during the exchange of a meso-Cl by another substituent is described m for example Dye and Pigments, 46, 2000, 163-168.

A further disadvantage of first synthesizing the meso-Cl dye is the fact that during the exchange of the chloride by the required substituent, chloride anions become available in the reaction medium, and may interfere in the reaction. When cationic cyanine dyes are prepared, the chloride anions may become an unwanted counter ion of the dye formed, or may compete with other, more preferred, counter ions. Since the type of counter ion may have an impact on the outcome of the dye formation reaction, for example by influencing the solubility of the cationic dye formed, it may be advantageous to avoid the presence of chloride anions during dye formation.
In EP 738 707, an intermediate according to the following formula

\[
\begin{align*}
\text{X}^- & \quad \text{R}'' \quad \text{N} \quad \text{R}''' \\
\text{H} & \quad \text{L} & \quad \text{H}
\end{align*}
\]

is used wherein \( R'' \) and \( R''' \) are independently an alkyl or aryl group, \( L \) is for example a 5- or 6-membered ring and \( X^- \) renders the intermediate neutral. From this intermediate, a cyanine dye having as meso-substituent \( -\text{NR}'' \text{R}''' \) is prepared in a single step. Using these intermediates no longer necessitates the preparation of a corresponding meso-Cl dye as intermediate dye. These intermediates are prepared by reacting an aniline compound, an orthoester and an iminium cation, said iminium cation according to the following formula, wherein \( R'' \), \( R''' \) independently represent an alkyl or aryl group and \( L \) is for example a 5- or 6-membered ring and \( X^- \) renders the molecule neutral:

\[
\begin{align*}
\text{R}'' & \quad \text{N} \quad \text{R}''' \\
\text{X}^- & \quad \text{H}_2\text{C} \quad \text{CH}_2
\end{align*}
\]

This reaction scheme is however not suitable to introduce substituents on the meso-position of a cyanine dye wherein \( R'' \) or \( R''' \), instead of alkyl or aryl groups, are electron withdrawing groups because no stable iminium cation according to the formula mentioned above with such electron withdrawing groups can be formed.

Therefore, this preparation method is for example not suitable to prepare, without going via the meso-Cl dye, the IR-dyes having the

EP-A 1 473 330 discloses a process for the synthesis of meso-substituted oxonole dyes wherein a \( \alpha \)-ketomethylene compound is reacted with a pyridinium compound. This process however is only suitable to prepare "open chain" oxonole dyes. An analogue methodology is used to prepare "open chain" indolinine dyes in JP-A 2001/151752.

Introducing electron withdrawing groups on a N-meso-substituent of cyanine dyes may be of interest, as described in the above mentioned applications EP-A 1 736 312 and WO2006/136543, to realize IR cyanine dyes forming a visible printout image after IR-exposure. It may also be of interest to enable the introduction of connecting groups on the meso-position, making the cyanine dye more useful for example to label biomolecules. Moreover, it may also enable the introduction of substituents on the meso-position of cyanine dyes which, upon exposure to actinic light, undergo a chemical transformation thereby releasing functional ingredients. Such released functional ingredients may for example participate in the image formation of imaging systems: as initiator of a polymerization reaction in photopolymer printing plate precursors; as solubilization inhibitor or accelerator in printing plate precursors having an imaging mechanism based on an increased (positive working) or decreased (negative working) solubilization of an imaging layer in a developer after (IR) exposure; or as coalescence agent in printing plate precursors having as imaging mechanism the coalescence of thermoplastic particles upon exposure to IR radiation.

There is thus a need for a preparation method of N-meso substituted cyanine, merocyanine or oxonole dyes wherein the N-meso substituent comprises electron withdrawals groups, without first preparing the corresponding meso-chloor dye.
SUMMARY OF THE INVENTION

It is an object of the present invention to provide new intermediate compounds enabling the preparation of N-meso substituted cyanine, merocyanine or oxonole dyes wherein the N-meso substituent comprises electron withdrawing groups and wherein such N-meso substituents are introduced at the intermediate level. These intermediates enable the formation of dyes having in the meso-position N-substituents comprising electron withdrawing groups without the need for further deπ vatization of the meso-substituent at the dye level. The method of preparation of the dyes provides high yields and a high level of purity of the end products and moreover offers an enhanced flexibility to prepare different dyes, i.e. cationic, anionic, zwitterionic, asymmetric or symmetric dyes, from the same intermediate without the need for further deπ vatization after chromophore formation, i.e. at the dye level. The method also offers the flexibility to select the counter ion of the dye to be formed at the intermediate level.

These objects are realized by the intermediate compounds as defined in independent claim 1 and the method of preparing the dyes as defined in independent claim 7. Other preferred embodiments of the invention are defined in the dependent claims.
DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to new intermediate compounds according to Formula I,

\[
\begin{array}{c}
\text{LG} \equiv \equiv \\
\text{R}^b \quad \text{R}^c \\
\text{A} \\
\text{LG'} \equiv \equiv \\
\end{array}
\]

wherein

- \( R^b \) and \( R^c \) independently represent a hydrogen atom or an optionally substituted alkyl group or represent the necessary atoms to form an optionally substituted ring structure;
- \( \text{LG} \) and \( \text{LG'} \) independently represent a leaving group precursor;
- \( A \) is selected from the list consisting of:
  - \(-\text{NR}^1\text{CO}-\text{R}^2\)
  - \(-\text{NR}^\text{SO}_2\text{R}^3\)
  - \(-\text{NR}^\text{SO}-\text{R}^5\)
  - \(-\text{NR}^\text{PO}-\text{R}^6\text{R}^7\)

wherein

- \( R^1 \) represents a hydrogen atom, an optionally substituted alkyl group, a \(-\text{SO}_3^-\) group, a \(-\text{COOR}^\text{R}\) group or an optionally substituted (hetero)aryl group, or \( R^1 \) together with at least one of \( R^9, R^{10} \) and \( R^{11} \) comprise the necessary atoms to form a ring structure;
- \( R^2 \) represents an optionally substituted alkyl or (hetero)aryl group, \(-\text{OR}^9, -\text{NR}^{10}\text{R}^{11} \) or \( \text{CF}_3 \);
- \( R^3 \) represents an optionally substituted alkyl group, an optionally substituted (hetero)aryl group, \(-\text{OR}^9, -\text{NR}^{10}\text{R}^{11} \) or...
-CF$_3$;

$^4$R represents a hydrogen atom, an optionally substituted alkyl group or an optionally substituted (hetero)aryl group;

$^5$R represents an optionally substituted alkyl group or an optionally substituted (hetero)aryl group;

$^6$and $^7$ independently represent an optionally substituted alkyl group, an optionally substituted aryl group or

-OR$^9$;

$^8$R represents an optionally substituted aryl group or an optionally substituted alkyl group, preferably an optionally substituted alpha-branched alkyl group;

$^9$R represents is an optionally substituted (hetero)aryl group or an optionally substituted alkyl group, preferably an optionally substituted branched alkyl group;

$^{10}$and $^{11}$ independently represent a hydrogen atom, an optionally substituted alkyl group, an optionally substituted (hetero)aryl group or represent the necessary atoms to form a cyclic structure.

Preferably, the substituent A in Formula I is selected from the list consisting of:

- $\text{-NR}^1\text{-CO-}R^2$
- $\text{-NR}^1\text{-SO}_2\text{-R}^3$

wherein $^1, ^2$ and $^3$ have the same meaning as described above for Formula I.
More preferably, the substituent A in Formula I is selected from the list consisting of:

\[
\begin{align*}
&\text{R}^1 \text{N} = \text{CO} \\
&\text{R}^9 \text{N} = \text{CO} \\
\end{align*}
\]

and

\[
\begin{align*}
&\text{R}^1 \text{N} = \text{S} \text{O} \\
&\text{R}^3 \text{N} = \text{S} \text{O} \\
\end{align*}
\]

wherein

R\(^1\) has the same meaning as described above for Formula I;
R\(^9\) represents an optionally substituted branched alkyl group; and
R\(^3\) represents \(-\text{CF}_3\), an optionally substituted aryl group or \(-\text{NR}^{10}\text{R}^{11}\) wherein R\(^{10}\) and R\(^{11}\) have the same meaning as described above for Formula I.

Particularly preferred, the substituent A in Formula I is selected from the list consisting of:

\[
\begin{align*}
&\text{R}^1 \text{N} = \text{CO} \\
&\text{R}^1 \text{N} = \text{CO} \\
&\text{R}^1 \text{N} = \text{S} \text{O} \\
&\text{R}^1 \text{N} = \text{S} \text{O} \\
&\text{F} \text{F} \text{F} \text{F} \\
&\text{R}^{10} \text{N} \text{R}^{11} \text{S} \text{O} \\
\end{align*}
\]

and
wherein \( R^1, R^{10} \) and \( R^{11} \) have the same meaning as in Formula I and \( S \) represents one or more optional substituents.

The one or more optional substituents \( S \) are preferably and independently selected from an optionally substituted alkyl group, halogen, alkoxy, cyano and \(-\text{CO}_2R^3\) wherein \( R^6 \) represents a hydrogen atom or an alkyl group.

The leaving group precursors \( LG \) and \( LG' \) are part of a group that is split off from the intermediate compound of Formula I during dye formation, as described in the second object of the invention.

Preferably, the leaving group precursor \( LG \) is selected from the list consisting of:

\[
\begin{array}{c}
\overset{R^{13}}{R^{12}} + \overset{N^*}{R^{14}} - \overset{O^*}{N^*},
\end{array}
\]

and the leaving group precursor \( LG' \) is selected from the list consisting of:

\[
\begin{array}{c}
\overset{R^{15}}{\overset{*}{N}} - \overset{R^{14}}{O^*} - \overset{R^{16}}{R^{17}}.
\end{array}
\]

wherein \( R^{12}, R^{13}, R^{14}, R^{15}, R^{16} \) and \( R^{17} \) independently represent a hydrogen atom, an optionally substituted alkyl group, an optionally substituted (hetero)aryl group or wherein \( R^{12} \) and \( R^{13} \) or \( R^{14} \) and \( R^{15} \) represent the necessary atoms to form a cyclic structure,

* represents the linking position of \( LG \) and \( LG' \) in Formula I.
Preferably, the intermediate compounds have a structure according to Formulae II, Ilia, IHb and IV, more preferably according to Formulae Ilia and IHb.

\[
\begin{align*}
&\text{Formula II} \\
&\text{Formula Ilia} \\
&\text{Formula IHb} \\
&\text{Formula IV}
\end{align*}
\]

wherein

- \(LG,\ LG'\) and \(A\) have the same meaning as in Formula I;
- \(R^{18}\) and \(R^{19}\) independently represent a hydrogen atom, an optionally substituted alkyl group, an optionally substituted (hetero)aryl group, \(-\text{CN}, -\text{COR}^{20}\) or \(-\text{CO}_2\text{R}^{20}\) wherein \(R^{20}\) represents a hydrogen atom or an alkyl group.

Highly preferred intermediates have a structure according to the following Formulae V to X:

\[
\begin{align*}
&\text{Formula V} \\
&\text{Formula VI}
\end{align*}
\]
wherein
A has the same meaning as in Formula I;
X\(^-\) renders the compound neutral,
R\(^{16}\) has the same meaning as described above.

Particularly preferred intermediate compounds have a structure according to Formula XI:

wherein R\(^{1}\) has the same meaning as described above for Formula I and X\(^-\) renders the formula neutral.

X\(^-\) in Formulae V, VIII, X and XI renders the intermediate compound neutral. Preferably X\(^-\) represents a halide anion, i.e. Cl\(^-\), Br\(^-\) or I\(^-\); a sulfonate group anion, e.g. CH\(_3\)SO\(_3\)\(^-\), CF\(_3\)SO\(_3\)\(^-\), p-toluene sulfonate; a tetrafluoroborate or a hexafluorophosphate anion.
Examples of intermediate compounds according to Formulae I to XI are given below.

INT-01

INT-02

INT-03

INT-04

INT-05

INT-06

INT-07

INT-08
INT-25

INT-26

INT-27

INT-28

INT-29

INT-30

INT-31

INT-32
An embodiment of the second object of the present invention is realized by a method for making a cyanme dye according to Formula XII,

![Formula XII](attachment:image.png)

wherein

- T and T' independently represent one or more substituents or an annulated ring;
- Z and Z' independently represent -0-, -S-, -CR\(^e\)\(R^f\)- or \(-\text{CH}=-\text{CH}-\) and wherein \(R^e\) and \(R^f\) independently represent an optionally substituted alkyl or aryl group;
- \(R^z\) and \(R'^z\) independently represent an optionally substituted alkyl group;
- \(R^b\) and \(R^c\) have the same meaning as in Formula I,
- \(R^a\) and \(R^d\) independently represent a hydrogen atom or an optionally substituted alkyl group;
- \(R^z\) and \(R^a\) or \(R^d\) and \(R'^z\) may represent the necessary atoms to form an optionally substituted 5- or 6-membered ring;
- \(X^-\) renders the dye neutral;

characterized in that the group A is directly incorporated in the cyanme dye by the reaction of an intermediate compound according to Formula I with an mdolium or azolium compound according to Formula XIII and an mdolium or azolium compound according to Formula XIV,
wherein

$T$, $T'$, $Z$, $Z'$, $R^z$, $R^z'$, $R$, $R'$, and $X$ have the same meaning as in Formula XII.

The one or more substituents $T$ and $T'$ may be independently selected from halogen, an optionally substituted alkyl group, an optionally substituted (hetero)alkyl group, an alkoxy group, a cyano group, $\text{CO}_2\text{R}^z$, $\text{CF}_3$ and $\text{SO}_2\text{R}^z'$ and wherein $\text{R}^z$ represents a hydrogen atom or an optionally substituted alkyl group and $\text{R}^z'$ represents an optionally substituted alkyl or an optionally substituted (hetero)aryl group.

According to a preferred embodiment, a cyanine dye according to Formula XVa or Formula XVb,

$T$, $T'$, $Z$, $Z'$, $R^z$, $R^z'$, $A$, and $X$ have the same meaning as in Formula XII,
is prepared by the reaction of an intermediate compound according to Formula Ilia or IHb with an indolium or azolium compound according to Formula XIII and an indolium or azolium compound according to Formula XIV.

In a highly preferred embodiment of the present invention a cyanine dye according to Formula XVI,

![Formula XVI](image)

wherein

- \( T, T', Z, Z', R^2, R^2' \) and \( X^- \) have the same meaning as in Formula XII and \( R^1 \) has the same meaning as in Formula I,

is prepared by the reaction of an intermediate compound according to Formula XI with an indolium or azolium compound according to Formula XIII and an indolium or azolium compound according to Formula XIV.

Typically, \( T, T', R^2 \) and \( R^2' \) in Formula XIII and XIV will determine whether the resulting dye is anionic, cationic or zwitterionic. Whether a cationic, anionic or zwitterionic cyanine dye is preferred, may depend on the application in which the cyanine dye will be used, for example the solubility of the dye in aqueous or non-aqueous media. When \( T, T', R^2 \) and \( R^2' \) are neutral substituents, the resulting cyanine dye according to Formulae XII, XVa, XVb or XVI will be cationic. By introducing anionic \( T, T', R^2 \) or \( R^2' \) groups, zwitterionic or anionic dyes, depending on the number and netto negative charge of those substituents, may be formed. It is also clear, that the method of the present invention to prepare cyanine
dyes according to Formulae XII, XVa, XVb or XVI offers an enhanced flexibility towards the preparation of different cyanine dyes, anionic, cationic or zwitterionic, from a single intermediate compound.

Anionic IR dyes are preferably prepared by the reaction of an intermediate compound according to the present invention described above with an mdolium or azolium compound according to Formula XVIIIa and an mdolium or azolium compound according to Formula XVIIIb,

\[ \text{Formula XVIIIa} \]

\[ \text{Formula XVIIIb} \]

wherein

\( T, T', Z \) and \( Z' \) have the same meaning as in Formula XII; \( n \) and \( n' \) independently represent an integer ranging from 1 to 3.

Anionic dyes may also be prepared by the reaction of an intermediate compound according to the present invention described above with an mdolium or azolium compound according to Formula XVIIIc and an mdolium or azolium compound according to Formula XVIIIId,
Cationic dyes are preferably prepared by the reaction of an intermediate compound according to the present invention described above with an indolium or azolium compound according to Formula XIXa and an indolium or azolium compound according to Formula XIXb,

wherein $T$, $T'$, $Z$, $Z'$, have the same meaning as in Formula XII;
$L$ and $L'$ represent 0 or 5;
$q$ and $q'$ independently represent an integer ranging from 1 to 2.

$m$ and $m'$ independently represent an integer ranging from 0 to 15.
The cyanine dyes according to Formulae XII, XVa, XVb and XVI obtained with the method described above, may be symmetric or asymmetric.

In a preferred embodiment, cyanine dyes according to Formulae XII, XVa, XVb and XVI are symmetric dyes wherein \( T = T' \), \( Z = Z' \), \( R^2 = R^2' \), \( R^a = R^d \) and \( R^b = R^c \).

Symmetric dyes are obtained with the method of the present invention described above by reacting an intermediate compound according to Formula I, wherein \( R^b = R^c \) or more preferably wherein \( R^b \) and \( R^c \) form a 5- or 6-membered ring as in the intermediates according to Formulae II, IIa, IIb, IV or XI with an indolium or azolium compound according to Formulae XIII or XIV. For the synthesis of a symmetric dye according to Formulae XII, XVa, XVb or XVI, approximately two equivalents of one indolium or azolium compound according to Formulae XIII or XIV is used for one equivalent of an intermediate compound according to the present invention.

It is clear that the method of the present invention to prepare cyanine dyes according to Formula XII, offers an enhanced flexibility towards the preparation of different cyanine dyes, i.e. symmetric or asymmetric, from the same intermediate compound.

If the intermediate compounds are reacted with two different compounds according to Formula XIII and XIV, a mixture of symmetric and asymmetric dyes is obtained. To obtain a pure asymmetric dye, an intermediate compound according to Formula I is reacted with a first compound according to Formula XIII followed by the isolation of a resulting mono-condensed products according to Formula XVII.
wherein \( A, T, T', R^z, R^a, R^b, R^c, LG' \) and \( X^- \) have the same meaning as in Formula XII.

Approximately one equivalent of the mono-condensed product according to Formula XVII is then further reacted with approximately one equivalent of a compound according to Formula XIV, different from the compound according to Formula XIII used to from the mono-condensed product, to obtain an asymmetric cyanine dye according to Formula XII.

In another embodiment of the second object of the invention a merocyanine according to Formula XX,

\[
\begin{align*}
\text{Formula XX} \\
\begin{array}{c}
\begin{array}{c}
T' \\
\end{array}
\end{array}
\end{align*}
\]

wherein
\[
A, R^b, R^c, R^d, R^z' \text{ and } T' \text{ have the same meaning as in Formula XII;} \\
Y \text{ represents } O, S \text{ or } NR^k; \\
Q \text{ represents } O, S, NR^k \text{ or } CONR^1 \text{ and wherein } R^k \text{ represents an}
\]
optionally substituted alkyl, benzyl or phenyl group and \( R^1 \) represents hydrogen, an optionally substituted alkyl or (hetero)aryl group; \( R^Y \) represents an optionally substituted alkyl or (hetero)aryl group,

is prepared by the reaction of an intermediate compound according to Formula I with a compound according to Formula XIII or XIV and a compound according to Formula XXI,

\[
\begin{align*}
&\text{Formula XXI} \\
&\text{wherein } Y, Q \text{ and } R^Y \text{ have the same meaning as in Formula XX.}
\end{align*}
\]

In still another embodiment of the present invention a dye according to Formula XXII,

\[
\begin{align*}
&\text{Formula XXII} \\
&\text{wherein} \\
&\text{\( R^Y, Q, Y, R^b, R^c \) have the same meaning as in Formula XX,}
\end{align*}
\]

is prepared by the reaction of an intermediate compound according to Formula I with a compound according to Formula XXI.
The intermediates of the present invention may be used to prepare other dyes by varying the one or more compounds to be reacted with the intermediate compounds.

Examples of dyes that may be synthesized with the method according to present invention are given below.

- D-O1
- D-02
- D-03
- D-04
- D-05
- D-06
D-07

D-08

D-09

D-10

D-II

D-12

D-13

D-14
A further object of the present invention is to provide a lithographic printing plate precursor comprising an IR-dye obtained with the method as described above.
EXAMPLES

Example 1

Preparation of INT-Ol

Step 1

A mixture of 1.2 mole of compound (1), 5 mole of (2) and 1.0 g of DBU (1,8-diazabicyclo(5,4,0)-7-undeceen) in toluene was heated to 100 °C. After methanol has been distilled off during 20 hours, the temperature of the mixture is increased to 165 °C, whereupon the methanol has been further distilled off for another 6 hours. After cooling and crystallisation of the mixture over night, the precipitate was washed in acetone, filtered and dried under vacuum. A crystalline powder of compound (3) was obtained with a yield of 38.6 %.

Step 2

0.51 mole of compound (3) was suspended in 300 ml CH₂Cl₂ followed by the dropwise addition of 0.612 mole of methyltriflate (Methyl
trifluoromethanesulfonate) during 10 minutes. After stirring the mixture for 1 hour at room temperature, compound (4) is precipitated with 2000 ml EtOAc (ethylacetate). After filtration, washing with EtOAc and drying under vacuum, compound (4) is obtained at a yield of 85%.

Step 3

\[
\begin{align*}
\text{CF}_3\text{SO}_3^- & \quad \text{Indoline} \\
\text{MeNH}_2 & \quad \text{MeOH} \\
\text{EtOAc} & \quad \text{CF}_3\text{SO}_3^-
\end{align*}
\]

0.279 mole of (4) was suspended in 150 ml ethanol at 22°C. During 10 minutes, 1.116 mole of MeNH\textsubscript{2} (methylamine) was added resulting in an increase of the temperature to 39°C. The mixture was stirred for 20 minutes at 35°C. After the addition of 200 ml acetic acid, resulting in an increase of the temperature to 56°C, the mixture was cooled to 40°C on ice followed by the addition of 0.418 mole of indoline. After stirring for 1 hour at room temperature, compound (5) was precipitated with 500 ml EtOAc (ethylacetate) while stirring for 30 minutes. After filtration, washing with 2 X 100 ml EtOAc, and drying under vacuum, compound (5) was obtained at a yield of 83%.

Step 4

\[
\begin{align*}
\text{CF}_3\text{SO}_3^- & \quad \text{Indoline} \\
\text{HOAc} & \quad \text{EtOAc} \\
\text{CF}_3\text{SO}_3^-
\end{align*}
\]

0.23 mole of compound (5) was suspended in 250 ml HOAc (Acetic Acid). After the addition of 0.46 mole of indoline while stirring, the
temperature of the reaction mixture was raised to 85°C. After 5 minutes, 200 ml of HOAc was added and the reaction mixture was maintained at 85 °C for another 45 minutes. Compound (6) was precipitated with 500 ml EtOAc (Ethylacetate) while stirring for 30 minutes. After filtration, washing with 2 x 100 ml of EtOAc, and drying under vacuum, compound (6) was obtained with a yield of 96%.

Step 5

![Chemical Structure](image1.png)

0.217 mole of compound (6) was suspended in 600 ml pyridine at 22°C. After adding 0.544 mole of compound (7) under stirring, the reaction mixture was kept at room temperature for 1 hour. After the addition of 500 ml EtOAc, the reaction mixture was stirred for another 30 minutes. After filtration, washing with 2 x 100 ml EtOAc, the filtrate was stirred in 500 ml EtOAc for 1 hour. After filtration, washing with 2 x 100 ml EtOAc and drying under vacuum, INT-Ol was obtained with a yield of 94%.

Example 2

Preparation of INT-Ol

Step 1

The same reaction scheme and conditions were used as in synthesis method 02, described above.
Step 2

0.1511 mole of compound (3) was dissolved in 200 ml of a 4 Volume/6 Volume mixture of Acetic Acid (HOAC)/Methanol (MeOH). At room temperature, 0.4632 mole of indolme (4) was added during 10 minutes under stirring. After stirring for 2 hours at room temperature, the reaction mixture was filtered off and the precipitate washed two times with 100 ml MeOH. Purification was performed by dissolving the precipitate in 500 ml methylene chloride (CH₂Cl₂) and stirring during 1 hour, followed by precipitation with 1500 ml MeOH. After filtration and drying under vacuum, compound (5) was obtained at a yield of 95%.

Step 3

0.1217 mole of compound (5) and 0.2678 mole of compound (6) were suspended in 600 ml toluene. The reaction mixture was brought in an oil bath having a temperature of 110 °C. After 2.5 hours at 110 °C,
the mixture was cooled to room temperature, followed by the addition to the mixture of 1500 ml MeOH. After stirring during 1 hour, the precipitate was filtered off, washed two times with 100 ml MeOH and dried under vacuum. Compound (7) was obtained with a yield of 83 %.

**Step 4**

![Diagram of reaction](image)

0.0364 mole of compound (7) and 0.0728 mole of DABCO (1,4-diazobicyclo (2,2,2) octane) were suspended in 100 ml N,N-dimethylacetamide. The reaction mixture was brought in an oil bath having a temperature of 120 °C. The reaction was carried out at 115 °C for 15 minutes, followed by cooling the mixture in ice.

500 ml of acetonitrile was added to the precipitate, the mixture was stirred for 1 hour at room temperature and filtered off. The precipitate was washed with 200 ml t-butyl methyl ether. After filtration and drying under vacuum, compound (8) was obtained at a yield of 57 %.

**Step 5**

![Diagram of reaction](image)

0.01299 mole of compound (8) was dissolved in 50 ml methylene chloride. 0.01559 mole of compound (9) (methyltriflate) was added
dropwise to the solution, after which the solution was stirred at room temperature during another 30 minutes. After precipitation with 125 ml ethyl acetate (EtOAc), the precipitate was purified by dissolving again in 100 ml methylene chloride and precipitation with 200 ml ethyl acetate. After filtration and drying under vacuum, INT-01 was obtained at a yield of 90%.

Example 3

Preparation of INT-02

To a suspension of compound (1) (50.5 g; 0.1 mole) in methylene chloride (400 ml) is added a 30% solution of sodium methanolate (NaOMe) in methanol (18 g; 0.1 mole). After stirring for 2 hours at room temperature, the suspension is filtered (removal of sodium trifluoromethane sulfonate). The resulting solution of compound (2) is treated with methane sulfonic acid (6.48 ml; 0.1 mole), followed by addition of ethyl acetate (21); upon filtration and drying, compound (3) is obtained as an orange powder (42.7 g; 94%).

Compound (3) (4.51 g; 10 mmole) is suspended in pyridine (150 ml) and compound (4) (6.54 g, 30 mmole) at room temperature. After
stirring for 2 hours, methanol (100 ml) is added, followed by ethyl acetate (1000 ml). Filtration and drying yields INT-02 (2.46 g; 44%) as a blue powder (Abs. Max. (methanol) = 600 nm).

Example 4

Preparation of INT-06

To a solution of INT-01 (5.0 g; 8.25 mmole) in a mixture of water (2 ml) and acetonitrile (18 ml) at room temperature is added acetic acid anhydride (1.55 ml; 1.65 mmole) and triethylamine (2.2 ml; 1.65 mmole). After heating at 80°C with stirring for 30 minutes, the reaction mixture is cooled to room temperature and water (80 ml) is added. The precipitate is filtered, digested in acetonitrile (20 ml) filtered, yielding INT-06 as a yellow powder (1.56 g; 54%).

Example 5

Preparation of INT-03
To a suspension of INT-06 (1.82 g ; 5.1 imole) in methanol (20 ml)
at room temperature is added indoline (611 mg ; 5.1 mmole) and an
50% aqueous solution of HBF₄ (895 mg ; 5.1 mmole). After 1 hour the
crude product is isolated by filtration. After dissolving the crude
intermediate in methylene chloride and precipitation with methanol,
followed by filtration and drying, one obtains pure INT-03 (2.19 g ;
79% ; Abs. Max. (methanol) = 600 nm).

Example 6

Preparation of INT-II

To a solution of INT-O1 (6.04 g ; 5 mmole) in CH₂Cl₂ (30 ml) is added
dimethyl ammonium dimethylcarbamate (DIMCARB) (2.8 ml ; 22 mmole).
After stirring for 30 minutes at room temperature, an additional
portion of DIMCARB (1.3 ml ; 10 mmole) is added twice. Upon addition
of methyl t.butyl ether (MTBE) (250 ml) INT-II precipitates.
Filtration, washing with MTBE (100 ml) and drying yields 3.14 g of
INT-II as a red powder (68% ; Abs. Max. (methanol)= 478 nm).
Example 7

Preparation of INT-30

To a solution of INT-Ol (5 g; 0.82 mmole) in acetonitrile (60 ml) is added MnCl₂ (6.8 g; 4.13 mmole). After stirring this suspension for 24 hours at room temperature, more acetonitrile (60 ml) and another batch of MnO₂ (6.8 g; 4.13 mmole) are added. After stirring for 2 hours, MnO₂ is filtered off on a glass filter. To the resulting solution is added ethyl acetate (2.0 l) to precipitate INT-30. After filtration and drying in vacuo, 3.11 g of INT-30 is obtained (63% yield; Abs. Max. (methanol)= 466/493 nm).

Example 8

Preparation of INT-20

To a solution of compound(l) (10 g; 19.7 mmole) and quinuclidine (2.2g; 19.7 mmole) in dimethyl sulfoxide (DMSO) (100 ml) are added
at room temperature triethylamine (16.4 ml; 118.2 mmole) and phthalic acid anhydride (17.5 g; 118.2 mmole). After stirring for 2 hours, INT-20 is precipitated by adding methanol (400 ml). Filtration and drying provides 6.97 g of INT-20 as a black powder (70%; Abs. Max. (methanol) = 602 nm).

**Example 9**

**Preparation of INT-19**

To a suspension of compound (1) (25.3 g; 0.05 mmole) in pyridine (50 ml) at room temperature is added triethylamine (27.7 ml; 0.2 mole) and benzoyl chloride (23.2 ml; 0.2 mole). After 30 minutes, ethyl acetate (300 ml) is added to precipitate INT-19. Filtration, digestion in water (100 ml) to remove salts and drying m vacuo results in 28.96 g of INT-19 (95%; Abs. Max. (methanol) = 609 nm).
Example 10
Preparation of INT-27

To a suspension of compound (1) (1.0 g; 1.97 mmole) in methylene chloride (50 ml) at room temperature are added quinuclidine (657 mg; 5.91 mmole), compound (2) (0.42 ml; 2.95 mmole), triethylamine (0.55 ml; 4.0 mmole) and p-toluene sulfonyl chloride (1.5 g; 7.88 mmole). After stirring for 1 hour, another portion of compound (2) (0.21 ml; 1.5 mmole) and p-toluene sulfonyl chloride (0.75 g; 3.94 mmole) is added. After 30 minutes, acetonitrile (50 ml) is added. Filtration removes residual starting material (with chloride counter ion). Upon addition of MTBE to this solution, crude INT-27 precipitates and is isolated by filtration. Digestion with water, filtration, washing with ethyl acetate and drying yields 1.1 g of INT-27 (83%; Abs. Max. (methanol) = 605 nm).
Preparation of D-Ol from INT-Ol prepared by the method of example 1

0.5 mole of compound (l) and 0.2 mole of INT-Ol were suspended in 600 ml CH₃CN (acetonitrile) at 22°C. After addition of 0.6 mole of HOAc (acetic acid) the temperature raised to 30°C. 1.0 mole of AC₂O (acetic acid anhydride) was added at 30°C, followed by the dropwise addition during 10 minutes of 0.8 mole of TEA (triethyl-amine). The reaction mixture was kept 80°C for 1.5 hour. After cooling down the temperature to room temperature, precipitation was induced by adding a mixture of 4000 ml EtOAc/40 ml water. The mixture was kept overnight, followed by filtration, washing with 2 x EtOAc. The filtrate was further stirred in 1000 ml Acetone followed by the addition of 0.02 mole of TEA. After filtration, washing with 2 x 100 ml acetone, and drying under vacuum, D-Ol was obtained with a yield of 87%.
Example 12

Preparation of D-Ol from INT-Ol prepared by the method of example 2

11.55 mmole of INT-Ol and 28.89 mmole of compound (1) were suspended in 50 ml of acetonitrile. 34.65 mmole of acetic acid and 57.75 mmole of acetic acid anhydride were added followed by the dropwise addition of 46.2 mmole of triethylamine. The mixture was heated to 80 °C and reacted during 3 hours. After cooling the mixture to room temperature, precipitation was carried out by adding a solution of 500 ml ethylacetate and 10 ml water. After filtration, the precipitate was washed with 200 ml acetone during 1 hour. After filtration and drying under vacuum, D-Ol was obtained with a yield of 72%.

Example 13

Preparation of D-02
1 mmole of D-Ol was dissolved in 10 ml MeOH. 1.1 mmole of ammonium acetate was added to the solution. After stirring the solution for 30 minutes, precipitation was carried out with a solution of 100 ml ethylacetate and 2 ml water. After filtration and drying under vacuum, D-02 was obtained with a yield of 81%.

Example 14

Preparation of D-39

To a solution of INT-Ol (3.03 g; 5 mmole) and compound(l) (3.6 g; 11 mmole) in acetonitrile (25 ml) at room temperature is added triethylamine (2.1 ml; 15 mmole). After stirring for 1 hour, filtering the precipitate, washing with acetonitrile (10 ml) and drying, 3.07 g of D-39 is obtained (yield = 85%; Abs. Max. (methanol) = 827 nm).
Example 15

Preparation of D-09

To a suspension of INT-02 (1.5 g; 2.7 mmole) and compound(l) (2.06 g; 5.98 mmole) in acetonitrile (15 ml) at room temperature is added acetic acid (0.46 ml; 8.1 mmole), acetic acid anhydride (1.26 ml; 13.5 mmole) and triethylamine (1.5 ml; 10.8 mmole). After heating at 80°C for 3 hours, cooling, addition of ethyl acetate containing 1% water (100 ml), filtration and drying yields D-09 (2.16 g; 79%; Abs. Max. (methanol) = 852 nm).

Example 16

Preparation of D-48
To a suspension of INT-03 (2.16 g; 3.9 mole) and compound(l) (2.4 g; 8.7 mmole) in acetonitrile at room temperature is added acetic acid (0.66 ml; 11.7 mmole), acetic acid anhydride (1.8 ml; 19.5 mmole), followed by heating the reaction mixture at 80°C for 15 minutes. After cooling to room temperature, the crude compound(2) is precipitated by adding a solution of methanol/water 1V/1V (60 ml). After isolation by filtration, the crude product is dissolved in methanol (30 ml). After filtration (to remove impurities), water (30 ml) is added to crystallize D-48. After filtration and drying, 790 mg of D-48 is obtained (30%; Abs. Max. (methanol) = 807 nm).

Example 17

Preparation of D-55

To a suspension of compound (l) (760 mg; 2.2 mmole) and INT-30 (603 mg; 1 mmole) in acetonitrile (10 ml) at room temperature is added acetic acid (0.17 ml; 3 mmole), acetic acid anhydride (0.47 ml; 5 mmole) and triethylamine (0.55 ml; 4 mmole). Under stirring, this mixture is heated at 80°C for 3 hours. After cooling to room temperature, ethyl acetate containing 1% water (100 ml) is added. After filtration and drying m vacuo, 697 mg of D-55 is obtained (70%; Abs. Max. (methanol) = 729 nm).
Example 18

Preparation of D-33

To a mixture of compound (1) (2.51 g; 8.8 mmole) and INT-20 (2.01 g; 4 mmole) in DMSO (20 ml) is added triethylamine (2.2 ml; 16 mmole) at room temperature. After stirring for 2 hours, a solution of 1% water in ethyl acetate (100 ml) is added. Filtration and drying provides 3.4 g of D-33 as a green powder (91%; Abs. Max. (methanol) = 833 nm).
Example 19

Preparation of D-31

To a suspension of compound(l) (6.27 g; 22 mmole) and INT-18 (5.21 g; 10 mmole) in dimethylacetamide (DMA) (50 ml) at room temperature is added t\text{\textpi}l ethylamine (5.5 ml; 40 mmole). After 1 hour, additional DMA (50 ml) is added. After stirring overnight at room temperature, filtration, digesting methyl acetate (100 ml), filtration and drying in vacuo provides 7.79 g of D-31 as a greenisch powder (74%; Abs. Max.(methanol) = 807 nm).
Example 20

Preparation of D-34

To a suspension of compound (1) (6.49 g; 22 mmole) and INT-19 (6.09 g; 10 mmole) in acetonitrile (30 ml) at room temperature are added acetic acid (1.7 ml; 30 mmole) and triethylamine (5.5 ml; 40 mmole).

After heating for 2 hours at 80°C and cooling to room temperature, the reaction product is precipitated by adding a solution of 1% water in ethyl acetate (60 ml). Filtration, digesting in ethyl acetate (50 ml), filtration and drying in vacuo results in 7.21 g of D-35 as a dark green powder (79%; Abs. Max. (methanol) = 820 nm).
[CLAIMS]

1. A compound according to Formula I,

\[
\begin{align*}
LG & \equiv A \equiv LG' \\
R^b & \quad R^c \\
R & \quad R \\
\end{align*}
\]

Formula I

wherein
R^b and R^c independently represent a hydrogen atom or an optionally substituted alkyl group or represent the necessary atoms to form an optionally substituted ring structure;
LG and LG' independently represent a leaving group precursor;
A is selected from the list consisting of:

- \(-NR^1-CO-R^2\)
- \(-NR^1-SO_2-R^3\)
- \(-NR^4-SO-R^5\)
- \(-NR^1-PO-R^6R^7\)

wherein
R^1 represents a hydrogen atom, an optionally substituted alkyl group, a \(-SO_3^-\) group, a \(-COOR^8\) group or an optionally substituted (hetero)aryl group, or R^1 together with at least one of R^9, R^10 and R^11 comprise the necessary atoms to form a ring structure;
R^2 represents an optionally substituted alkyl or (hetero)aryl group, \(-OR^9\), \(-NR^{10}R^{11}\) or \(-CF_3\);
R^3 represents an optionally substituted alkyl group, an optionally substituted (hetero)aryl group, \(-OR^9\), \(-NR^{10}R^{11}\) or \(-CF_3\);
R^4 represents a hydrogen atom, an optionally substituted alkyl group or an optionally substituted (hetero)aryl group;
R represents an optionally substituted alkyl group or an optionally substituted (hetero) aryl group;
R⁶ and R⁷ independently represent an optionally substituted alkyl group, an optionally substituted aryl group or -OR⁹;
R⁸ represents an optionally substituted aryl group or an optionally alkyl group;
R⁹ represents is an optionally substituted (hetero) aryl group or an optionally alkyl group;
R¹⁰ and R¹¹ independently represent a hydrogen atom, an optionally substituted alkyl group, an optionally substituted (hetero) aryl group or represent the necessary atoms to form a cyclic structure.

2. The compound according to claim 1 wherein A is selected from the list consisting of:

\[
\begin{align*}
\text{R}^1 & \quad \text{OR}^9 \\
\text{N} & \quad \text{O} \\
\text{R}^1 & \quad \text{R}^3 \\
\text{N} & \quad \text{S} \quad \text{O} \\
\text{and} & \\
\text{R}^1 & \quad \text{OR}^9 \\
\text{N} & \quad \text{O} \\
\text{R}^1 & \quad \text{R}^3 \\
\text{N} & \quad \text{S} \quad \text{O}
\end{align*}
\]

where:

- R¹ has the same meaning as in claim 1, R⁹ represents an optionally substituted branched alkyl group and R³ represents -CF₃, an optionally substituted aryl group or -NR¹⁰R¹¹ wherein R¹⁰ and R¹¹ have the same meaning as in Formula I.
3. The compound according to claim 1 or 2 wherein the leaving group precursor \( \text{LG} \) is selected from the list consisting of:

\[
\begin{align*}
\text{R}^{13} \\
\text{R}^{12} - \text{N}^* \\
\text{R}^{14} - \text{N}^* \\
\text{O}^* & \text{ and } \text{S}^*
\end{align*}
\]

and the leaving group precursor \( \text{LG}' \) is selected from the list consisting of:

\[
\begin{align*}
\text{R}^{15} \\
\text{N} - \text{R}^{14} \\
\text{O} - \text{R}^{16} & \text{ and } \text{S} - \text{R}^{17}
\end{align*}
\]

wherein \( \text{R}^{12}, \text{R}^{13}, \text{R}^{14}, \text{R}^{15}, \text{R}^{16} \text{ and } \text{R}^{17} \) independently represent a hydrogen atom, an optionally substituted alkyl group, an optionally substituted (hetero)aryl group or wherein \( \text{R}^{12} \text{ and } \text{R}^{13} \) or \( \text{R}^{14} \text{ and } \text{R}^{15} \) represent the necessary atoms to form a cyclic structure,

* represents the linking position of \( \text{LG} \) and \( \text{LG}' \) in Formula I.

4. The compound according to any of the preceding claims having a structure according to Formulae II, IIa, IIb and IV,
wherein

LG, LG' and A have the same meaning as in Formula I;

R$^{18}$ and R$^{19}$ independently represent a hydrogen atom, an optionally substituted alkyl group, an optionally substituted (hetero)aryl group, -CN, -CO$_2$R$^{20}$ or COR$^{21}$ wherein R$^{20}$ represents a hydrogen atom or an alkyl group and R$^{21}$ represents a hydrogen atom, an optionally substituted alkyl group or an optionally substituted (hetero)aryl group.

5. The compound according to any of the preceding claims having a structure according to Formula Ilia or IHb,

wherein

LG, LG' and A have the same meaning as in Formula I.

6. The compound according to any of the preceding claims having a structure according to Formula V,
wherein
A has the same meaning as in formula I;
X^- renders the compound neutral.

1. The compound according to any of the preceding claims having a structure according to Formula XI,

![Formula XI]

wherein
R^1 has the same meaning as in Formula I and X^- renders the compound neutral.

8. A method for making a cyanine dye according to Formula XII

![Formula XII]

wherein
T and T' independently represent one or more substituents or an annulated ring;
Z and Z' independently represent -O-, -S-, -CH=CH- or -CR^6R^f-
and wherein R^e and R^f independently represent an optionally substituted alkyl or aryl group;
R\textsubscript{z} and R\textsubscript{z'} independently represent an optionally substituted alkyl group;
R\textsubscript{b} \text{ and } R\textsubscript{c} have the same meaning as in claim 1.
R\textsubscript{a} \text{ and } R\textsubscript{d} independently represent a hydrogen atom or an optionally substituted alkyl group;
R\textsubscript{z} \text{ and } R\textsubscript{a}, R\textsubscript{d} \text{ and } R\textsubscript{z'} may represent the necessary atoms to form an optionally substituted 5- or 6-membered ring;
X\textsuperscript{-} renders the dye neutral,

comprising the step of reacting an intermediate compound as defined in any one of claims 1 to 7 with an indolium or azolium compound according to Formula XIII and an indolium or azolium compound according to Formula XIV,

wherein
T, T', Z, Z', R\textsubscript{z}, R\textsubscript{z'}, R\textsubscript{a}, R\textsubscript{b} and X\textsuperscript{-} have the same meaning as in Formula XII.

9. The method according to claim 8 wherein the indolium or azolium compounds have a structure according to Formula XVIII\textsubscript{a} and Formula XVIII\textsubscript{b},
10. The method according to claim 8 wherein the indolium or azolium compounds have a structure according to Formula XIXa and Formula XIXb,

wherein
\( T, T', Z \) and \( Z' \) have the same meaning as in Formula XXII;
\( n \) and \( n' \) independently represent an integer ranging from 1 to 3.

11. The method according to claim 8 wherein the indolium or azolium compounds according to Formulae XIII and XIV are identical.
12. A lithographic printing plate precursor comprising an IR-dye obtained with the method as defined in claims 8 to 11.
### A. CLASSIFICATION OF SUBJECT MATTER

INV. C07C251/14 C07C251/20 C07D403/08 C07D403/10 C07D413/08 C07D413/10 C07D417/08 C07D417/10

### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07C C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

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### D

Further documents are listed in the continuation of Box C

See patent family annex

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