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(54) Titre : PROCEDE DE PREPARATION DE NAPHTHALOCYANINES

(54) Title: METHOD OF PREPARING NAPHTHALOCYANINES

(57) **Abrégé/Abstract:**

A method of preparing a naphthalocyanine is provided. The method comprises the steps of: (i) providing a tetrahydronaphthalic anhydride; (ii) converting said tetrahydronaphthalic anhydride to a benzisoindolenine; and (iii) macrocyclizing said benzisoindolenine to form a naphthalocyanine.



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(54) Title: METHOD OF PREPARING NAPHTHALOCYANINES

(57) Abstract: A method of preparing a naphthalocyanine is provided. The method comprises the steps of: (i) providing a tetrahydronaphthalic anhydride; (ii) converting said tetrahydronaphthalic anhydride to a benzisoindolenine; and (iii) macrocyclizing said benzisoindolenine to form a naphthalocyanine.

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METHOD OF PREPARING NAPHTHALOCYANINES

Field of the Invention

The present application relates generally to an improved method of synthesizing naphthalocyanines. It has been developed primarily to reduce the cost of existing naphthalocyanine syntheses and to facilitate large-scale preparations of these compounds.

Background of the Invention

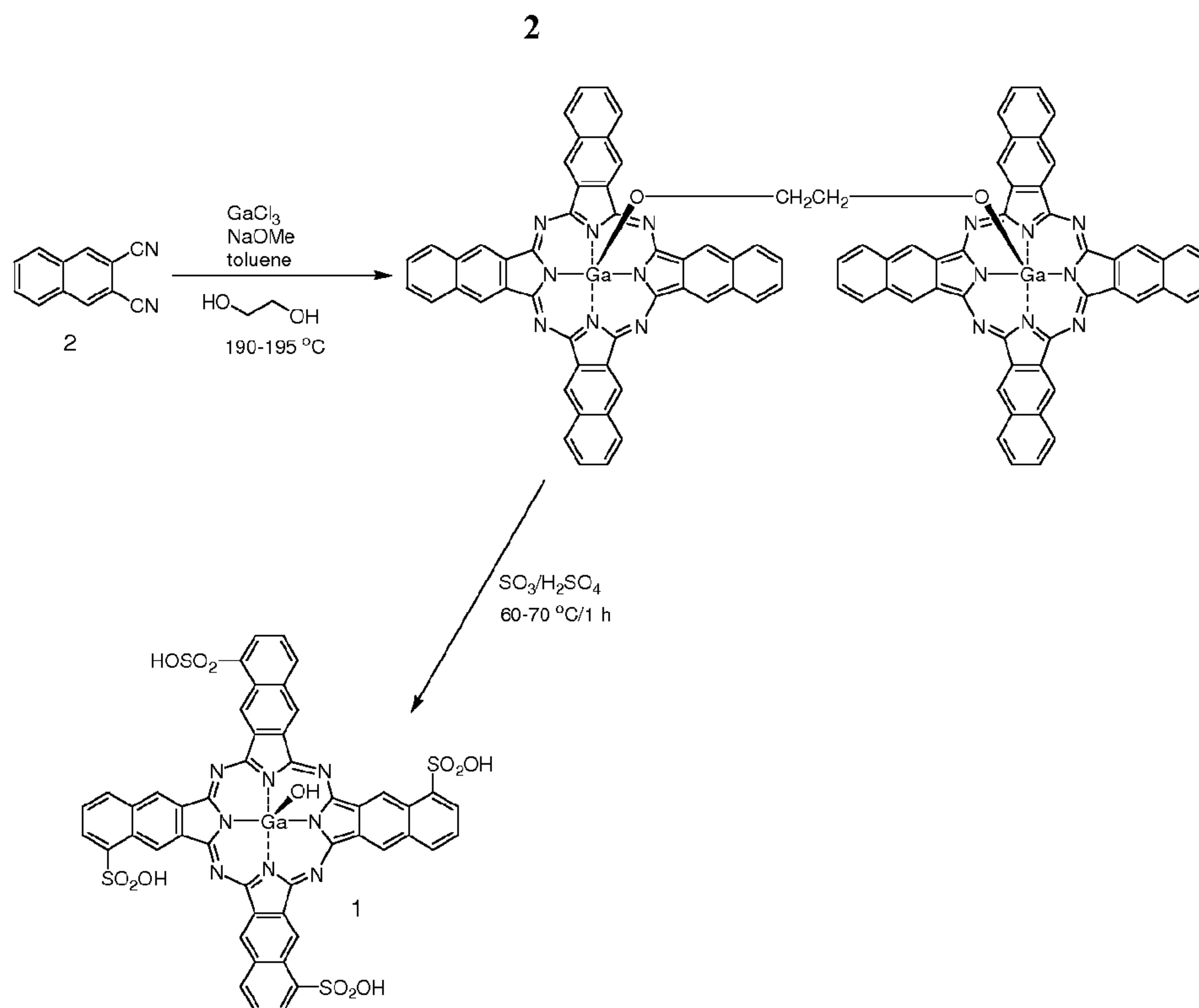
We have described previously the use of naphthalocyanines as IR-absorbing dyes. Naphthalocyanines, and particularly gallium naphthalocyanines, have low absorption in the visible range and intense absorption in the near-IR region (750-810 nm). Accordingly, naphthalocyanines are attractive compounds for use in invisible inks. The Applicant's US Patent Nos. 7,148,345 and 7,122,076 (the contents of which are herein incorporated by reference) describe in detail the use of naphthalocyanine dyes in the formulation of inks suitable for printing invisible (or barely visible) coded data onto a substrate. Detection of the coded data by an optical sensing device can be used to invoke a response in a remote computer system. Hence, the substrate is interactive by virtue of the coded data printed thereon.

The Applicant's netpage and Hyperlabel® systems, which makes use of interactive substrates printed with coded data, are described extensively in the cross-referenced patents and patent applications above (the contents of which are herein incorporated by reference).

In the anticipation of widespread adoption of netpage and Hyperlabel® technologies, there exists a considerable need to develop efficient syntheses of dyes suitable for use in inks for printing coded data. As foreshadowed above, naphthalocyanines and especially gallium naphthalocyanines are excellent candidates for such dyes and, as a consequence, there is a growing need to synthesize naphthalocyanines efficiently and in high yield on a large scale.

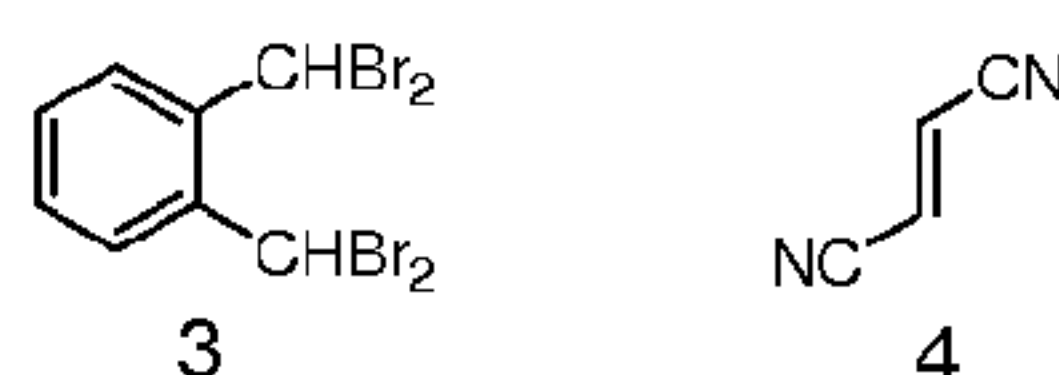
Naphthalocyanines are challenging compounds to synthesize on a large scale. In US Patent Nos. 7,148,345 and 7,122,076, we described an efficient route to naphthalocyanines via macrocyclization of naphthalene-2,3-dicarbonitrile. Scheme 1 shows a route to the sulfonated gallium naphthalocyanine 1 from naphthalene-2,3-dicarbonitrile 2, as described in US 7,148,345.

30



Scheme 1

However, a problem with this route to naphthalocyanines is that the starting material 2 is expensive. Furthermore, naphthalene-2,3-dicarbonitrile 2 is prepared from two expensive building blocks: tetrabromo-*o*-xylene 3 and fumaronitrile 4, neither of which can be readily prepared in multi-kilogram quantities.



Accordingly, if naphthalocyanines are to be used in large-scale applications, there is a need to improve on existing syntheses.

10

Summary of the Invention

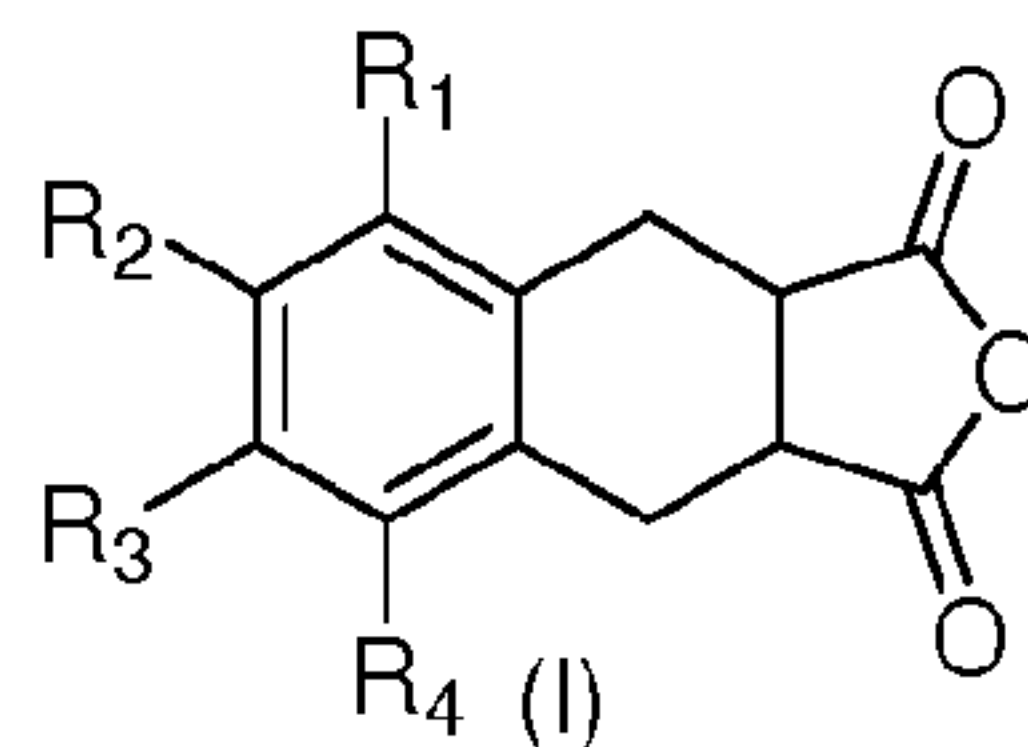
In a first aspect, there is provided a method of preparing a naphthalocyanine comprising the steps of:

- (i) providing a tetrahydronaphthalic anhydride;
- (ii) converting said tetrahydronaphthalic anhydride to a benzisindolenine; and
- (iii) macrocyclizing said benzisindolenine to form a naphthalocyanine.

15

Optionally, the tetrahydronaphthalic anhydride is of formula (I):

3



wherein:

R_1 , R_2 , R_3 and R_4 are each independently selected from hydrogen, hydroxyl, C_{1-20} alkyl, C_{1-20} alkoxy, amino, C_{1-20} alkylamino, di(C_{1-20} alkyl)amino, halogen, cyano, thiol, C_{1-20} alkylthio, nitro,

- 5 C_{1-20} alkylcarboxy, C_{1-20} alkylcarbonyl, C_{1-20} alkoxy carbonyl, C_{1-20} alkylcarbonyloxy, C_{1-20} alkylcarbonylamino, C_{5-20} aryl, C_{5-20} arylalkyl, C_{5-20} aryloxy, C_{5-20} arylalkoxy, C_{5-20} heteroaryl, C_{5-20} heteroaryloxy, C_{5-20} heteroarylalkoxy or C_{5-20} heteroarylalkyl.

Optionally, R_1 , R_2 , R_3 and R_4 are all hydrogen.

- 10 Optionally, step (ii) comprises a one-pot conversion from the tetrahydronaphthalic anhydride to a benzoindolenine salt. This one-pot conversion facilitates synthesis of naphthalocyanines via the route described above and greatly improves yields and scalability.

Optionally, the benzoindolenine salt is a nitrate salt although other salts (*e.g.* benzene sulfonate salt) are of course within the scope of the present invention.

- 15 Optionally, the one-pot conversion is effected by heating with a reagent mixture comprising ammonium nitrate.

Optionally, the reagent mixture comprises at least 2 equivalents of ammonium nitrate with respect to the tetrahydronaphthalic anhydride.

Optionally, the reagent mixture comprises urea.

Optionally, the reagent mixture comprises at least one further ammonium salt.

- 20 Optionally, the further ammonium salt is selected from: ammonium sulfate and ammonium benzenesulfonate

Optionally, the reagent mixture comprises a catalytic amount of ammonium molybdate.

Optionally, the heating is within a temperature range of 150 to 200°C.

The reaction may be performed in the presence of or in the absence of a solvent.

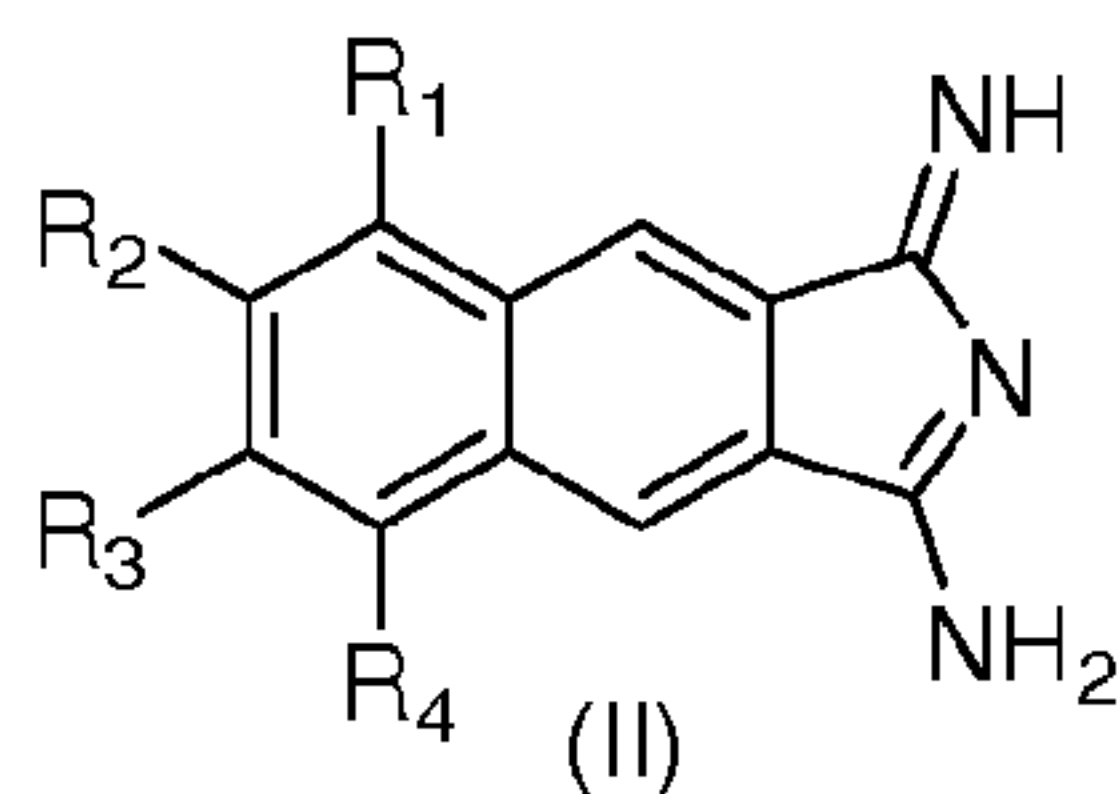
- 25 Optionally, heating is in the presence of an aromatic solvent. Examples of suitable solvents are nitrobenzene, biphenyl, diphenyl ether, mesitylene, anisole, phenetole, dichlorobenzene, trichlorobenzene and mixtures thereof.

Optionally, the benzoindolenine is liberated from the benzoindolenine salt using a base. Sodium methoxide is an example of a suitable base although the skilled person will be readily

- 30 aware of other suitable bases.

Optionally, the benzoindolenine is of formula (II):

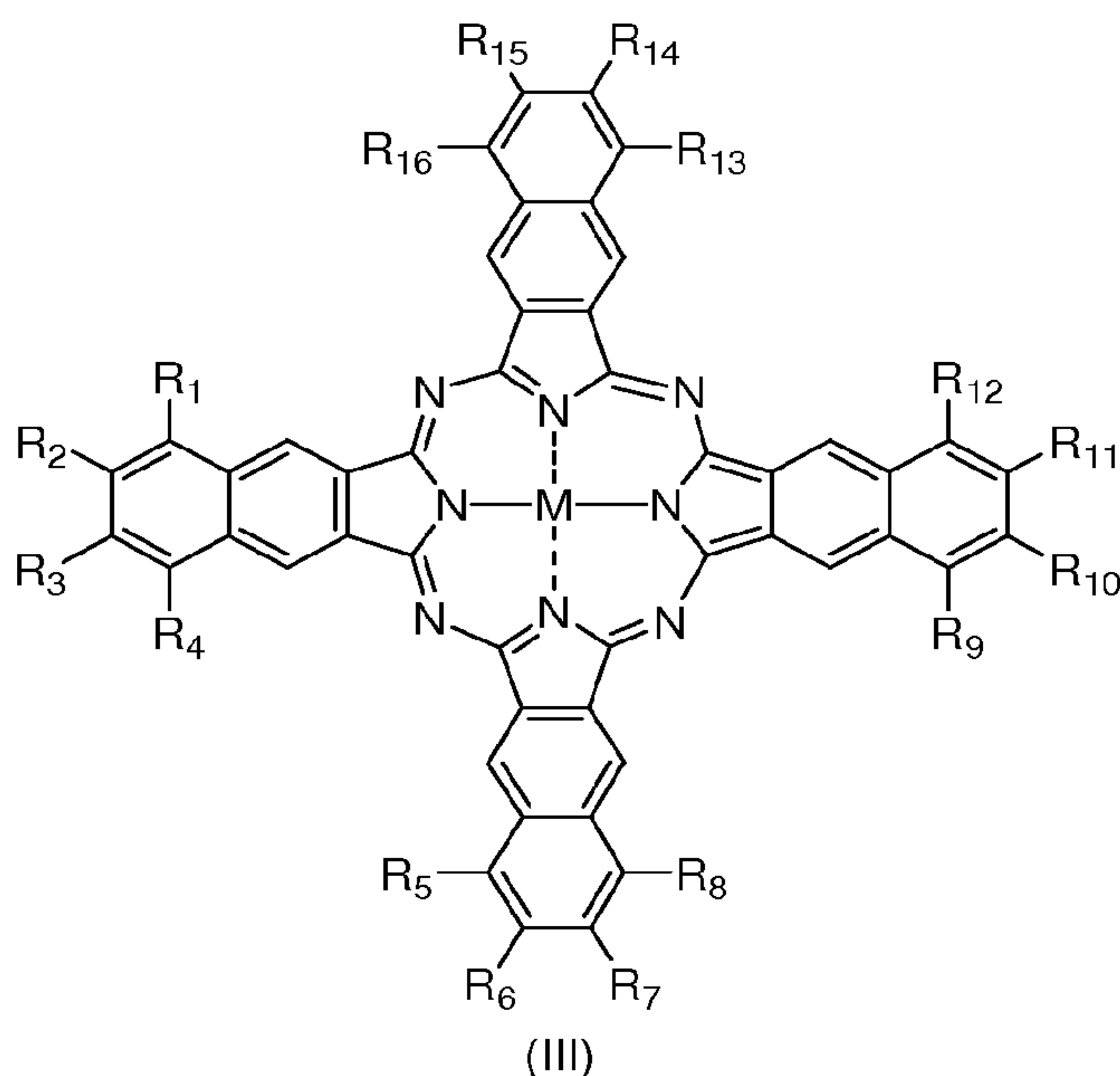
4



wherein:

- R₁, R₂, R₃ and R₄ are each independently selected from hydrogen, hydroxyl, C₁₋₂₀ alkyl, C₁₋₂₀ alkoxy, amino, C₁₋₂₀ alkylamino, di(C₁₋₂₀ alkyl)amino, halogen, cyano, thiol, C₁₋₂₀ alkylthio, nitro, C₁₋₂₀ alkylcarboxy, C₁₋₂₀ alkylcarbonyl, C₁₋₂₀ alkoxycarbonyl, C₁₋₂₀ alkylcarbonyloxy, C₁₋₂₀ alkylcarbonylamino, C₅₋₂₀ aryl, C₅₋₂₀ arylalkyl, C₅₋₂₀ aryloxy, C₅₋₂₀ arylalkoxy, C₅₋₂₀ heteroaryl, C₅₋₂₀ heteroaryloxy, C₅₋₂₀ heteroarylalkoxy or C₅₋₂₀ heteroarylalkyl.

Optionally, the naphthalocyanine is of formula (III):



10

wherein:

- R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉, R₁₀, R₁₁, R₁₂, R₁₃, R₁₄, R₁₅ and R₁₆ are each independently selected from hydrogen, hydroxyl, C₁₋₂₀ alkyl, C₁₋₂₀ alkoxy, amino, C₁₋₂₀ alkylamino, di(C₁₋₂₀ alkyl)amino, halogen, cyano, thiol, C₁₋₂₀ alkylthio, nitro, C₁₋₂₀ alkylcarboxy, C₁₋₂₀ alkylcarbonyl, C₁₋₂₀ alkoxycarbonyl, C₁₋₂₀ alkylcarbonyloxy, C₁₋₂₀ alkylcarbonylamino, C₅₋₂₀ aryl, C₅₋₂₀ arylalkyl, C₅₋₂₀ aryloxy, C₅₋₂₀ arylalkoxy, C₅₋₂₀ heteroaryl, C₅₋₂₀ heteroaryloxy, C₅₋₂₀ heteroarylalkoxy or C₅₋₂₀ heteroarylalkyl;

M is absent or selected from Si(A¹)(A²), Ge(A¹)(A²), Ga(A¹), Mg, Al(A¹), TiO, Ti(A¹)(A²), ZrO, Zr(A¹)(A²), VO, V(A¹)(A²), Mn, Mn(A¹), Fe, Fe(A¹), Co, Ni, Cu, Zn, Sn, Sn(A¹)(A²), Pb,

20 Pb(A¹)(A²), Pd and Pt;

A¹ and A² are axial ligands, which may be the same or different, and are selected from –OH, halogen or –OR^q;

R^q is selected from C₁₋₁₆ alkyl, C₅₋₂₀ aryl, C₅₋₂₀ arylalkyl, C₁₋₂₀ alkylcarbonyl, C₁₋₂₀ alkoxy carbonyl or Si(R^x)(R^y)(R^z); and

5 R^x, R^y and R^z may be the same or different and are selected from C₁₋₂₀ alkyl, C₅₋₂₀ aryl, C₅₋₂₀ arylalkyl, C₁₋₂₀ alkoxy, C₅₋₂₀ aryloxy or C₅₋₂₀ arylalkoxy;

Optionally, R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉, R₁₀, R₁₁, R₁₂, R₁₃, R₁₄, R₁₅ and R₁₆ are all hydrogen.

10 Optionally, M is Ga(A¹), such as Ga(OCH₂CH₂OCH₂CH₂OCH₂CH₂OMe); that is where R^q is CH₂CH₂OCH₂CH₂OCH₂CH₂OMe. For the avoidance of doubt, ethers such as CH₂CH₂OCH₂CH₂OCH₂CH₂OMe fall within the definition of alkyl groups as specified hereinbelow. Gallium compounds are preferred since they have excellent lightfastness, strong absorption in the near-IR region, and are virtually invisible to the human eye when printed on a page.

15 Optionally, step (iii) comprises heating the benzoindolenine in the presence of a metal compound, such as AlCl₃ or GaCl₃ or a corresponding metal alkoxide. The reaction may be performed in the absence of or in the presence of a suitable solvent, such as toluene, nitrobenzene *etc.* When a metal alkoxide is used, the reaction may be catalyzed with a suitable base, such as sodium methoxide. Alcohols, such as triethylene glycol monomethyl ether or glycol may also be
20 present to assist with naphthalocyanine formation. These alcohols may end up as the axial ligand of the naphthalocyanine or they may be cleaved from the metal under the reaction conditions. The skilled person will readily be able to optimize the conditions for naphthalocyanine formation from the benzoindolenine.

Optionally, the method further comprises the step of sulfonating said naphthalocyanine.
25 Sulfonate groups are useful for solubilizing the naphthalocyanines in ink formulations, as described in our earlier US Patents Nos. 7,148,345 and 7,122,076.

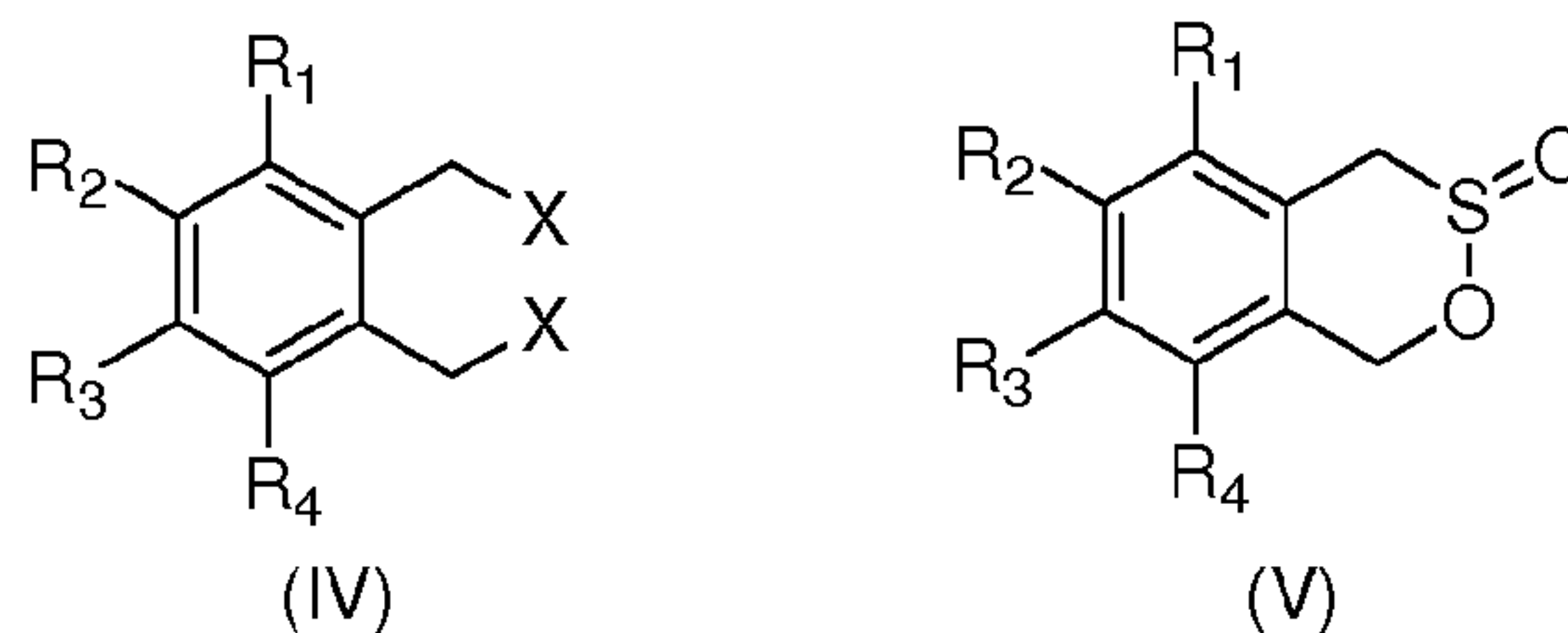
In a second aspect, there is provided a method of effecting a one-pot conversion of a tetrahydronaphthalic anhydride to a benzoindolenine salt, said method comprising heating said tetrahydronaphthalic anhydride with a reagent mixture comprising ammonium nitrate.

30 This transformation advantageously obviates a separate dehydrogenation step to form the naphthalene ring system. The ammonium nitrate performs the dual functions of oxidation (dehydrogenation) and isoindolenine formation.

The isoindolenine salts generated according to the second aspect may be used in the synthesis of naphthalocyanines. Hence, this key reaction provides a significant improvement in
35 routes to naphthalocyanines.

In general, optional features of this second aspect mirror the optional features described above in respect of the first aspect.

In a third aspect, there is provided a method of preparing a sultine of formula (V) from a dihalogeno compound of formula (IV)



the method comprising reacting the dihalogeno compound (IV) with a hydroxymethanesulfinate salt in a DMSO solvent so as to prepare the sultine (V);

wherein:

R_1 , R_2 , R_3 and R_4 are each independently selected from hydrogen, hydroxyl, C_{1-20} alkyl, C_{1-20} alkoxy, amino, C_{1-20} alkylamino, di(C_{1-20} alkyl)amino, halogen, cyano, thiol, C_{1-20} alkylthio, nitro, C_{1-20} alkylcarboxy, C_{1-20} alkylcarbonyl, C_{1-20} alkoxy carbonyl, C_{1-20} alkylcarbonyloxy, C_{1-20} alkylcarbonylamino, C_{5-20} aryl, C_{5-20} arylalkyl, C_{5-20} aryloxy, C_{5-20} arylalkoxy, C_{5-20} heteroaryl, C_{5-20} heteroaryloxy, C_{5-20} heteroarylalkoxy or C_{5-20} heteroarylalkyl; and X is Cl, Br or I.

The method according to the third aspect surprisingly minimizes polymeric by-products and improves yields, when compared to literature methods for this reaction employing DMF as the solvent. These advantages are amplified when the reaction is performed on a large scale (*e.g.* at least 0.3 molar, at least 0.4 molar or at least 0.5 molar scale).

Optionally, NaI is used to catalyze the coupling reactions when X is Cl or Br.

Optionally, a metal carbonate base (*e.g.* Na_2CO_3 , K_2CO_3 , Cs_2CO_3 *etc*) is present.

Optionally, the hydroxymethanesulfinate salt is sodium hydroxymethanesulfinate (RongaliteTM).

Optionally, R_1 , R_2 , R_3 and R_4 are all hydrogen.

Optionally, the method comprises the further step of reacting the sultine (V) with an olefin at elevated temperature (*e.g.* about 80°C) to generate a Diels-Alder adduct.

Optionally, the olefin is maleic anhydride and said Diels-Alder adduct is a tetrahydronaphthalic anhydride.

Optionally, the tetrahydronaphthalic anhydride is used as a precursor for naphthalocyanine synthesis, as described herein.

Optionally, the naphthalocyanine synthesis proceeds via conversion of the tetrahydronaphthalic anhydride to a benzisindolenine, as described herein.

Brief Description of the Drawings

The invention will now be described in detail with reference to the following drawings, in which:

Figure 1 is a ^1H NMR spectrum of the crude sultine 10 in d_6 -DMSO;

Figure 2 is a ^1H NMR spectrum of the anhydride 8 in d_6 -DMSO;

Figure 3 is a ^1H NMR spectrum of the crude benzoindolenine salt 12 in d_6 -DMSO;

Figure 4 is an expansion of the aromatic region of the ^1H NMR spectrum shown in Figure

5 3;

Figure 5 is a ^1H NMR spectrum of the benzoindolenine 7 in d_6 -DMSO.

Figure 6 is an expansion of the aromatic region of the ^1H NMR spectrum shown in Figure

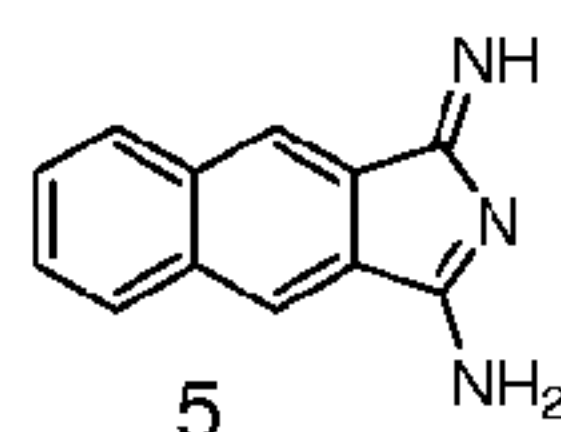
5; and

Figure 7 is a UV-VIS spectrum of naphthalocyanatogallium methoxytriethyleneoxide in

10 NMP.

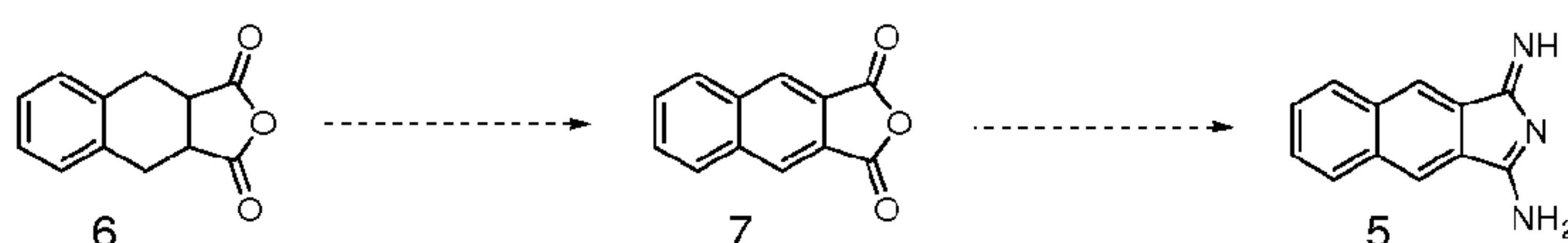
Detailed Description

As an alternative to dicyanitriles, the general class of phthalocyanines is known to be prepared from isoindolenines. In US 7,148,345, we proposed the benzoindolenine 5 as a possible precursor to naphthalocyanines.



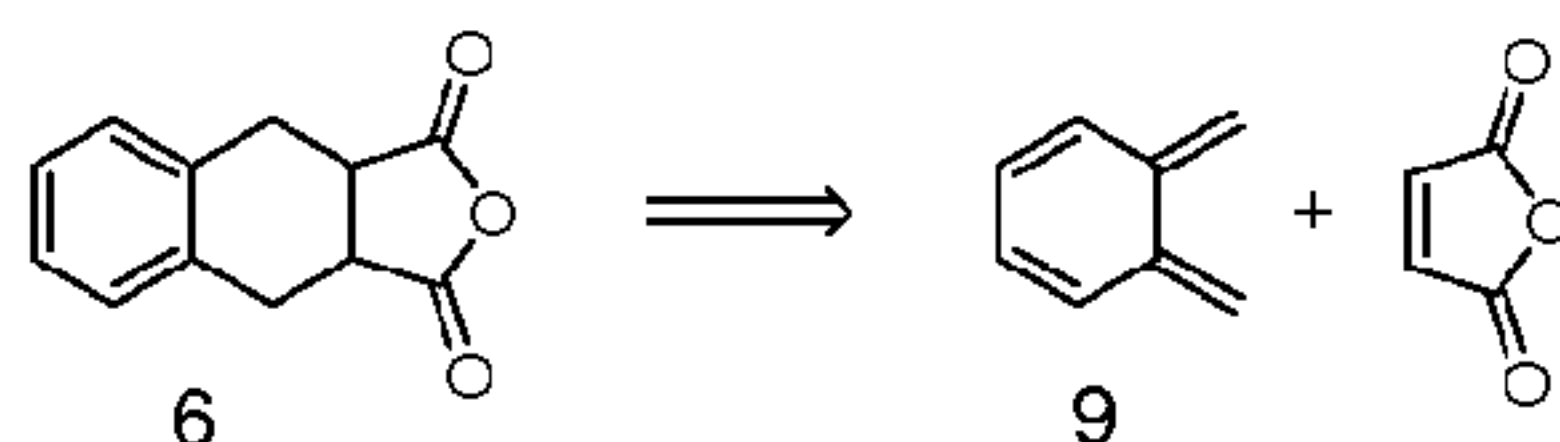
However, efficient syntheses of the benzoindolenine 5 were unknown in the literature, and it was hitherto understood that dicyanitriles, such as naphthalene-2,3-dicyanitrile 2, were the only viable route to naphthalocyanines.

Nevertheless, with the potentially prohibitive cost of naphthalene-2,3-dicyanitrile 2, the present inventors sought to explore a new route to the benzoindolenine 5, as outlined in Scheme 2.



Scheme 2

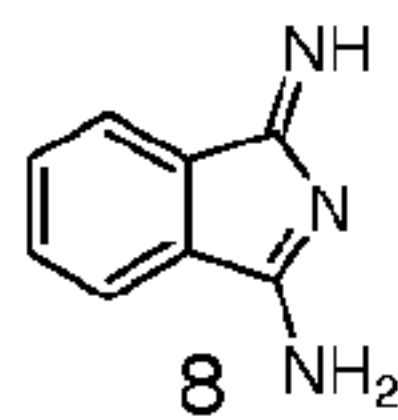
Tetrahydronaphthalic anhydride 6 was an attractive starting point, because this is a known Diels-Alder adduct which may be synthesized via the route shown in Scheme 3.



Scheme 3

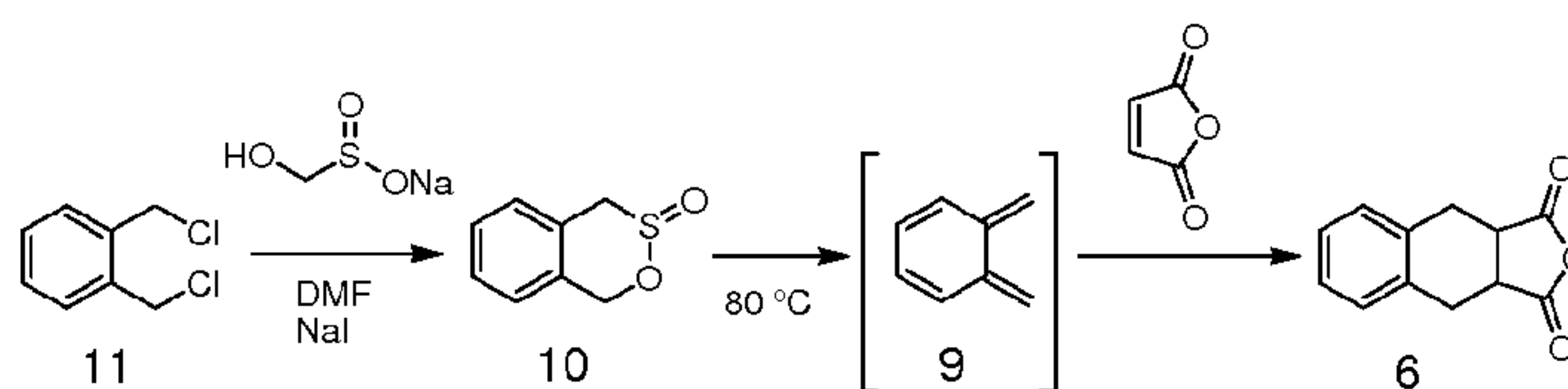
Referring to Scheme 2, it was hoped that the conversion of naphthalic anhydride 7 to the benzoindolenine 5 would proceed analogously to the known conversion of phthalic anhydride to the isoindolenine 8, as described in WO98/31667.

8



However, a number of problems remained with the route outlined in Scheme 2. Firstly, the dehydrogenation of tetrahydronaphthalic anhydride 6 typically requires high temperature catalysis. Under these conditions, tetrahydronaphthalic anhydride 6 readily sublimes resulting in very poor yields. Secondly, the preparation of tetrahydronaphthalic anhydride 6 on a large scale was not known. Whilst a number of small-scale routes to this compound were known in the literature, these generally suffered either from poor yields or scalability problems.

The use of sultines as diene precursors is well known and 1,4-dihydro-2,3-benzoxathiin-3-oxide 10 has been used in a synthesis of 6 on a small scale (Hoey, M. D.; Dittmer, D. A. *J. Org. Chem.* 1991, 56, 1947-1948). As shown in Scheme 4, this route commences with the relatively inexpensive dichloro-*o*-xylene 11, but the feasibility of scaling up this reaction sequence is limited by the formation of undesirable polymeric by-products in the sultine-forming step. The formation of these by-products makes reproducible production of 6 in high purity and high yield difficult.

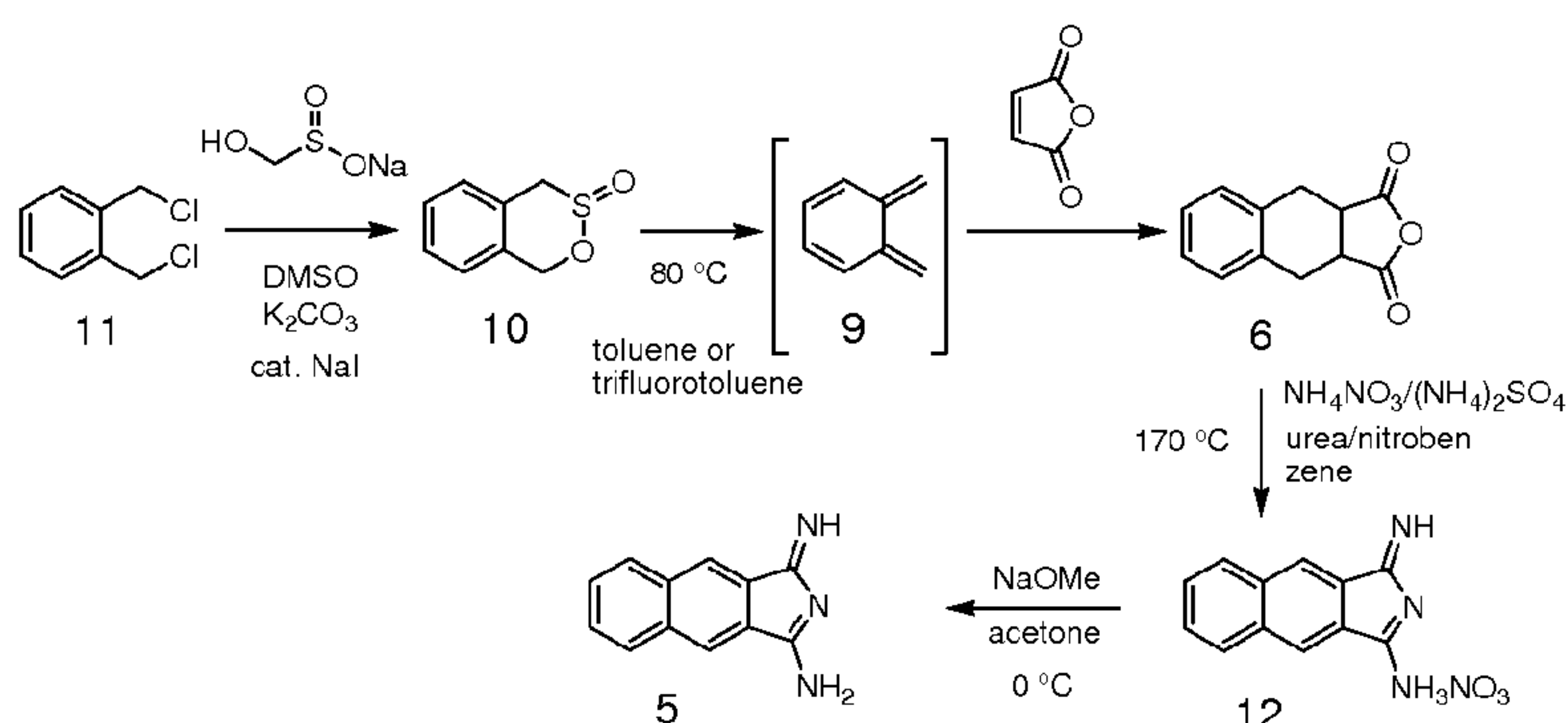


Scheme 4

Nevertheless, the route outlined in Scheme 4 is potentially attractive from a cost standpoint, since dichloro-*o*-xylene 11 and maleic anhydride are both inexpensive materials.

Whilst the reaction sequence shown in Schemes 4 and 2 present significant synthetic challenges, the present inventors have surprisingly found that, using modified reaction conditions, the benzisindolenine 5 can be generated on a large scale and in high yield. Hence, the present invention enables the production of naphthalocyanines from inexpensive starting materials, and represents a significant cost improvement over known syntheses, which start from naphthalene-2,3-dicarbonitrile 2.

Referring to Scheme 5, there is shown a route to the benzisindolenine 5, which incorporates two synthetic improvements in accordance with the present invention.



Scheme 5

Unexpectedly, it was found that by using DMSO as the reaction solvent in the conversion of 11 into 10, the reaction rate and selectivity for the formation of sultine 10 increases significantly.

5 This is in contrast to known conditions (Hoey, M. D.; Dittmer, D. A. *J. Org. Chem.* 1991, 56, 1947-1948) employing DMF as the solvent, where the formation of undesirable polymeric side-products is a major problem, especially on a large scale. Accordingly, the present invention provides a significant improvement in the synthesis of tetrahydronaphthalic anhydride 6.

The present invention also provides a significant improvement in the conversion of
10 tetrahydronaphthalic anhydride 6 to the benzoindolenine 5. Surprisingly, it was found that the ammonium nitrate used for this step readily effects oxidation of the saturated ring system as well as converting the anhydride to the isoindolenine. Conversion to a tetrahydroisoindolenine was expected to proceed smoothly, in accordance with the isoindolenine similar systems described in WO98/31667. However, concomitant dehydrogenation under these reaction conditions
15 advantageously provided a direct one-pot route from the tetrahydronaphthalic anhydride 6 to the benzoindolenine salt 12. This avoids problematic and low-yielding dehydrogenation of the tetrahydronaphthalic anhydride 6 in a separate step. Subsequent treatment of the salt 12 with a suitable base, such as sodium methoxide, liberates the benzoindolenine 5. As a result of these improvements, the entire reaction sequence from 11 to 5 is very conveniently carried out, and
20 employs inexpensive starting materials and reagents (Scheme 5).

The benzoindolenine 5 may be converted into any required naphthalocyanine using known conditions. For example, the preparation of a gallium naphthalocyanine from benzoindolenine 5 is exemplified herein. Subsequent manipulation of the naphthalocyanine macrocycle may also be performed in accordance with known protocols. For example, sulfonation
25 may be performed using oleum, as described in US Patent Nos. 7,148,345 and 7,122,076.

Hitherto, the use of tetrahydronaphthalic anhydride 6 as a building block for naphthalocyanine synthesis had not previously been reported. However, it has now been shown that tetrahydronaphthalic anhydride 6 is a viable intermediate in the synthesis of these important compounds. Moreover, it is understood by the present inventors that the route shown in Scheme 5
30 represents the most cost-effective synthesis of benzoindolenines 5.

The term "aryl" is used herein to refer to an aromatic group, such as phenyl, naphthyl or triptycenylyl. C₆₋₁₂ aryl, for example, refers to an aromatic group having from 6 to 12 carbon atoms, excluding any substituents. The term "arylene", of course, refers to divalent groups corresponding to the monovalent aryl groups described above. Any reference to aryl implicitly includes arylene,
35 where appropriate.

The term "heteroaryl" refers to an aryl group, where 1, 2, 3 or 4 carbon atoms are replaced by a heteroatom selected from N, O or S. Examples of heteroaryl (or heteroaromatic) groups include pyridyl, benzimidazolyl, indazolyl, quinolinyl, isoquinolinyl, indolinyl, isoindolinyl, indolyl, isoindolyl, furanyl, thiophenyl, pyrrolyl, thiazolyl, imidazolyl, oxazolyl, isoxazolyl,

pyrazolyl, isoxazolonyl, piperazinyl, pyrimidinyl, piperidinyl, morpholinyl, pyrrolidinyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrimidinyl, benzopyrimidinyl, benzotriazole, quinoxalinyl, pyridazyl, coumarinyl *etc.* The term “heteroarylene”, of course, refers to divalent groups corresponding to the monovalent heteroaryl groups described above. Any
 5 reference to heteroaryl implicitly includes heteroarylene, where appropriate.

Unless specifically stated otherwise, aryl and heteroaryl groups may be optionally substituted with 1, 2, 3, 4 or 5 of the substituents described below.

Where reference is made to optionally substituted groups (*e.g.* in connection with aryl groups or heteroaryl groups), the optional substituent(s) are independently selected from C₁₋₈ alkyl,
 10 C₁₋₈ alkoxy, $-(OCH_2CH_2)_dOR^d$ (wherein *d* is an integer from 2 to 5000 and R^{*d*} is H, C₁₋₈ alkyl or C(O)C₁₋₈ alkyl), cyano, halogen, amino, hydroxyl, thiol, -SR^{*v*}, -NR^{*u*}R^{*v*}, nitro, phenyl, phenoxy, -CO₂R^{*v*}, -C(O)R^{*v*}, -OCOR^{*v*}, -SO₂R^{*v*}, -OSO₂R^{*v*}, -SO₂OR^{*v*}, -NHC(O)R^{*v*}, -CONR^{*u*}R^{*v*}, -CONR^{*u*}R^{*v*}, -SO₂NR^{*u*}R^{*v*}, wherein R^{*u*} and R^{*v*} are independently selected from hydrogen, C₁₋₂₀ alkyl, phenyl or phenyl-C₁₋₈ alkyl (*e.g.* benzyl). Where, for example, a group contains more than one substituent,
 15 different substituents can have different R^{*u*} or R^{*v*} groups.

The term “alkyl” is used herein to refer to alkyl groups in both straight and branched forms. Unless stated otherwise, the alkyl group may be interrupted with 1, 2, 3 or 4 heteroatoms selected from O, NH or S. Unless stated otherwise, the alkyl group may also be interrupted with 1, 2 or 3 double and/or triple bonds. However, the term “alkyl” usually refers to alkyl groups having
 20 double or triple bond interruptions. Where “alkenyl” groups are specifically mentioned, this is not intended to be construed as a limitation on the definition of “alkyl” above.

Where reference is made to, for example, C₁₋₂₀ alkyl, it is meant the alkyl group may contain any number of carbon atoms between 1 and 20. Unless specifically stated otherwise, any reference to “alkyl” means C₁₋₂₀ alkyl, preferably C₁₋₁₂ alkyl or C₁₋₆ alkyl.

The term “alkyl” also includes cycloalkyl groups. As used herein, the term “cycloalkyl” includes cycloalkyl, polycycloalkyl, and cycloalkenyl groups, as well as combinations of these with linear alkyl groups, such as cycloalkylalkyl groups. The cycloalkyl group may be interrupted with 1, 2 or 3 heteroatoms selected from O, N or S. However, the term “cycloalkyl” usually refers to cycloalkyl groups having no heteroatom interruptions. Examples of cycloalkyl groups include
 30 cyclopentyl, cyclohexyl, cyclohexenyl, cyclohexylmethyl and adamantyl groups.

The term “arylalkyl” refers to groups such as benzyl, phenylethyl and naphthylmethyl.

The term “halogen” or “halo” is used herein to refer to any of fluorine, chlorine, bromine and iodine. Usually, however, halogen refers to chlorine or fluorine substituents.

Where reference is made herein to “a naphthalocyanine”, “a benzisindolenine”, “a
 35 tetrahydronaphthalic anhydride” *etc.*, this is understood to be a reference to the general class of compounds embodied by these generic names, and is not intended to refer to any one specific compound. References to specific compounds are accompanied with a reference numeral.

Chiral compounds described herein have not been given stereo-descriptors. However, when compounds may exist in stereoisomeric forms, then all possible stereoisomers and mixtures thereof are included (*e.g.* enantiomers, diastereomers and all combinations including racemic mixtures *etc.*).

5 Likewise, when compounds may exist in a number of regioisomeric or tautomeric forms, then all possible regioisomers, tautomers and mixtures thereof are included.

For the avoidance of doubt, the term “a” (or “an”), in phrases such as “comprising a”, means “at least one” and not “one and only one”. Where the term “at least one” is specifically used, this should not be construed as having a limitation on the definition of “a”.

10 Throughout the specification, the term “comprising”, or variations such as “comprise” or “comprises”, should be construed as including a stated element, integer or step, but not excluding any other element, integer or step.

The invention will now be described with reference to the following drawings and examples. However, it will of course be appreciated that this invention may be embodied in many
15 other forms without departing from the scope of the invention, as defined in the accompanying claims.

Example 1

20 *1,4-dihydro-2,3-benzoxathiin-3-oxide 10*

Sodium hydroxymethanesulfinate (Rongalite™) (180 g; 1.17 mol) was suspended in DMSO (400 mL) and left to stir for 10 min. before dichloro-*o*-xylene (102.5 g; 0.59 mol), potassium carbonate (121.4 g; 0.88 mol) and sodium iodide (1.1 g; 7 mmol) were added consecutively. More DMSO (112 mL) was used to rinse residual materials into the reaction mixture before the whole was
25 allowed to stir at room temperature. The initial endothermic reaction became mildly exothermic after around 1 h causing the internal temperature to rise to *ca.* 32-33 °C. The reaction was followed by TLC (ethyl acetate/hexane, 50:50) and found to be complete after 3 h. The reaction mixture was diluted with methanol/ethyl acetate (20:80; 400 mL) and the solids were filtered off, and washed with more methanol/ethyl acetate (20:80; 100 mL, 2 × 50 mL). The filtrate was transferred to a
30 separating funnel and brine (1 L) was added. This caused more sodium chloride from the product mixture to precipitate out. The addition of water (200 mL) redissolved the sodium chloride. The mixture was shaken and the organic layer was separated and then the aqueous layer was extracted further with methanol/ethyl acetate (20:80; 200 mL, 150 mL, 250 mL). The combined extracts were dried (Na₂SO₄) and rotary evaporated (bath 37-38 °C). More solvent was removed under high
35 vacuum to give the sultine 10 as a pale orange liquid (126 g) that was found by ¹H NMR spectroscopy to be relatively free of by-product but containing residual DMSO and ethyl acetate (Figure 1).

Example 2*Tetrahydronaphthalic anhydride 6*

The crude sultine from above (126 g) was diluted in trifluorotoluene (100 mL) and then added to a preheated (bath 80 °C) suspension of maleic anhydride (86 g; 0.88 mol) in trifluorotoluene (450 mL). The residual sultine was washed with more trifluorotoluene into the reaction mixture and then the final volume was made up to 970 mL. The reaction mixture was heated at 80 °C for 15 h, more maleic anhydride (28.7 g; 0.29 mol) was added and then heating was continued for a further 8 h until TLC showed that the sultine had been consumed. While still at 80 °C, the solvent was removed by evaporation with a water aspirator and then the residual solvent was removed under high vacuum. The moist solid was triturated with methanol (200 mL) and filtered off, washing with more methanol (3 × 100 mL). The tetrahydronaphthalic anhydride 6 was obtained as a fine white crystalline solid (75.4 g; 64% from 10) after drying under high vacuum at 60-70 °C for 4 h.

Example 3

The sultine was prepared from dichloro-*o*-xylene (31.9 g; 0.182 mol), as described in Example 2, and then reacted with maleic anhydride (26.8 g; 0.273 mol) in toluene (300 mL total volume) as described above. This afforded the tetrahydronaphthalic anhydride 6 as a white crystalline solid (23.5 g; 64%).

Example 4*1-amino-3-iminobenz[*f*]isoindolenine nitrate salt 12*

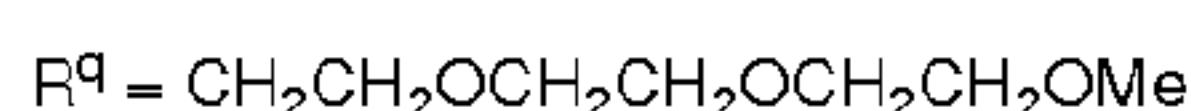
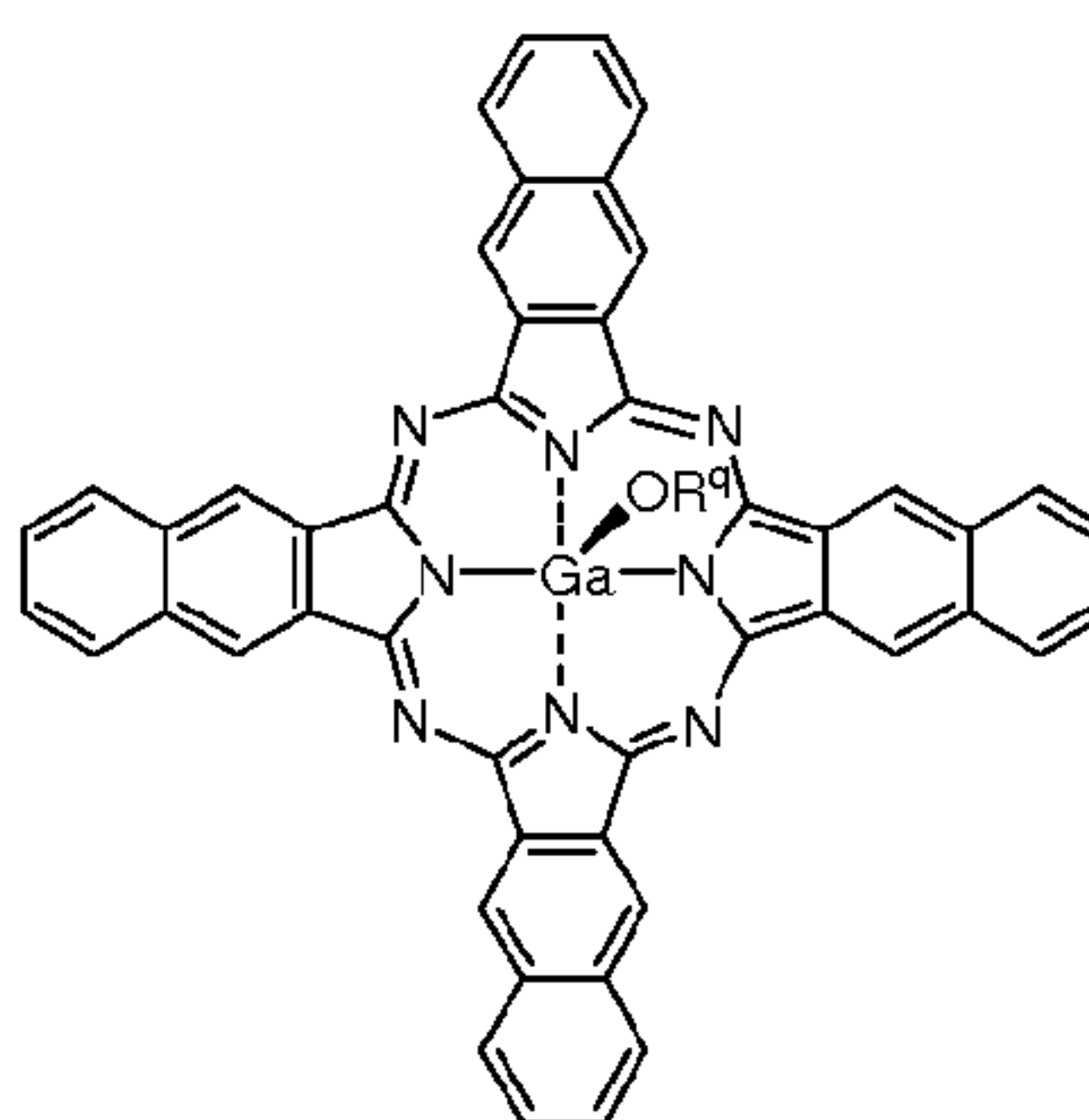
Urea (467 g; 7.78 mol) was added to a mechanically stirred mixture of ammonium sulfate (38.6 g; 0.29 mol), ammonium molybdate (1.8 g) and nitrobenzene (75 mL). The whole was heated with a heating mantle to *ca.* 130 °C (internal temperature) for 1 h causing the urea to melt. At this point the anhydride 6 (98.4 g; 0.49 mol) was added all at once as a solid. After 15 min ammonium nitrate (126.4 g; 1.58 mol) was added with stirring (internal temperature 140 °C) accompanied by substantial gas evolution. The reaction temperature was increased to 170-175 °C over 45 min and held there for 2 h 20 min. The viscous brown mixture was allowed to cool to *ca.* 100 °C and then methanol (400 mL) was slowly introduced while stirring. The resulting suspension was poured on a sintered glass funnel, using more methanol (100 mL) to rinse out the reaction flask. After removing most of the methanol by gravity filtration, the brown solid was sucked dry and then washed with more methanol (3 × 200 mL, 50 mL), air-dried overnight and dried under high vacuum in a warm water bath for 1.5 h. The benzisindolenine salt 12 was obtained as a fine brown powder (154.6 g) and was found by NMR analysis to contain urea (5.43 ppm) and other salts (6.80 ppm). This material was used directly in the next step without further purification.

Example 5*1-amino-3-iminobenz[*f*]isoindolenine 7*

The crude nitrate salt 12 (154.6 g) was suspended in acetone (400 mL) with cooling in an ice/water bath to 0 °C. Sodium methoxide (25% in methanol; 284 ml; 1.3 mol) was added slowly dropwise via a dropping funnel at such a rate as to maintain an internal temperature of 0-5 °C. Upon completion of the addition, the reaction mixture was poured into cold water (2 × 2 L) in two 2 L conical flasks. The mixtures were then filtered on sintered glass funnels and the solids were washed thoroughly with water (250 mL; 200 mL for each funnel). The fine brown solids were air-dried over 2 days and then further dried under high vacuum to give the benzoindolenine 5 as a fine brown powder (69.1 g; 73%).

10 Example 6

Naphthalocyanatogallium methoxytriethyleneoxide



15 Gallium chloride (15.7 g; 0.089 mol) was dissolved in anhydrous toluene (230 mL) in a 3-neck flask (1 L) equipped with a mechanical stirrer, heating mantle, thermometer, and distillation outlet. The resulting solution was cooled in an ice/water bath to 10 °C and then sodium methoxide in methanol (25%; 63 mL) was added slowly with stirring such that the internal temperature was maintained below 25 °C thereby affording a white precipitate. The mixture was then treated with
 20 triethylene glycol monomethyl ether (TEGMME; 190 mL) and then the whole was heated to distill off all the methanol and toluene (3 h). The mixture was then cooled to 90-100 °C (internal temperature) by removing the heating mantle and then the benzoindolenine 5 from the previous step (69.0 g; 0.35 mol) was added all at once as a solid with the last traces being washed into the reaction vessel with diethyl ether (30 mL). The reaction mixture was then placed in the preheated
 25 heating mantle such that an internal temperature of 170 °C was established after 20 min. Stirring was then continued at 175-180 °C for a further 3 h during which time a dark green/brown colour appeared and the evolution of ammonia took place. The reaction mixture was allowed to cool to ca. 100 °C before diluting with DMF (100 mL) and filtering through a sintered glass funnel under gravity overnight. The moist filter cake was sucked dry and washed consecutively with DMF (80
 30 mL), acetone (2 × 100 mL), water (2 × 100 mL), DMF (50 mL), acetone (2 × 50 mL; 100 mL) and diethyl ether (100 mL) with suction. After brief air drying, the product was dried under high

vacuum at 60-70 °C to constant weight. Naphthalocyanatogallium methoxytriethyleneoxide was obtained as a microcrystalline dark blue/green solid (60.7 g; 76%); λ_{max} (NMP) 771 nm (Figure 7).

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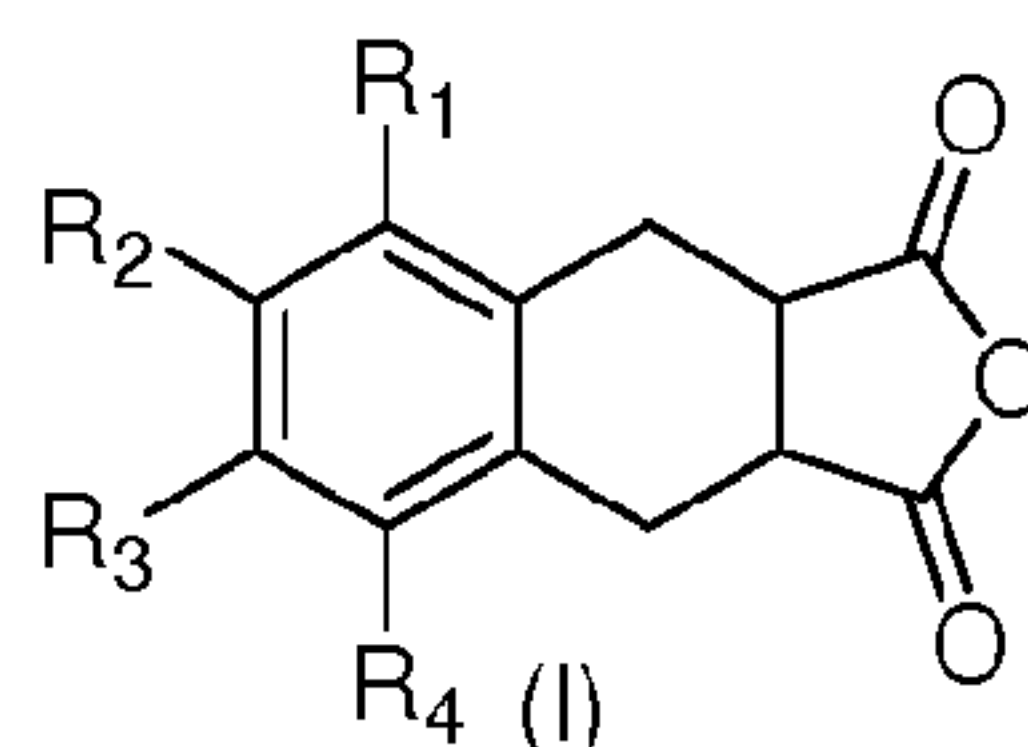
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CLAIMS

1. A method of preparing a naphthalocyanine comprising the steps of:
- 5 (i) providing a tetrahydronaphthalic anhydride;
- (ii) converting said tetrahydronaphthalic anhydride to a benzoindolenine; and
- (iii) macrocyclizing said benzoindolenine to form a naphthalocyanine.

2. The method of claim 1, wherein said tetrahydronaphthalic anhydride is of formula (I):



10

wherein:

- R_1 , R_2 , R_3 and R_4 are each independently selected from hydrogen, hydroxyl, C_{1-20} alkyl, C_{1-20} alkoxy, amino, C_{1-20} alkylamino, di(C_{1-20} alkyl)amino, halogen, cyano, thiol, C_{1-20} alkylthio, nitro, C_{1-20} alkylcarboxy, C_{1-20} alkylcarbonyl, C_{1-20} alkoxy carbonyl, C_{1-20} alkylcarbonyloxy, C_{1-20} alkylcarbonylamino, C_{5-20} aryl, C_{5-20} arylalkyl, C_{5-20} aryloxy, C_{5-20} arylalkoxy, C_{5-20} heteroaryl, C_{5-20} heteroaryloxy, C_{5-20} heteroarylalkoxy or C_{5-20} heteroarylalkyl.

15

3. The method of claim 2, wherein R_1 , R_2 , R_3 and R_4 are all hydrogen.

20

4. The method of claim 1, wherein step (ii) comprises a one-pot conversion from the tetrahydronaphthalic anhydride to a benzoindolenine salt.

5. The method of claim 4, wherein said salt is a nitrate salt.

25

6. The method of claim 4, wherein said one-pot conversion is effected by heating with a reagent mixture comprising ammonium nitrate.

7. The method of claim 6, wherein said reagent mixture comprises at least 2 equivalents of ammonium nitrate with respect to said tetrahydronaphthalic anhydride.

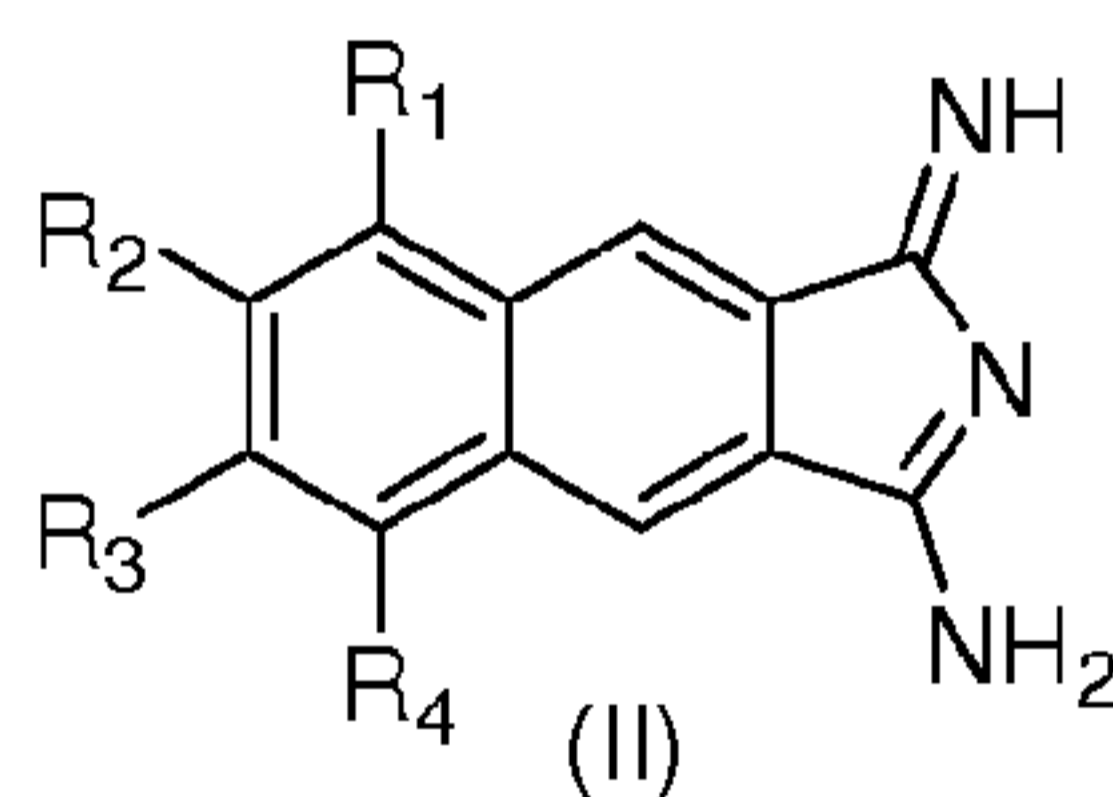
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8. The method of claim 6, wherein said reagent mixture comprises urea.

9. The method of claim 6, wherein said reagent mixture comprises at least one further ammonium salt.

35

10. The method of claim 9, wherein said at least one further ammonium salt is selected from: ammonium sulfate and ammonium benzenesulfonate
11. The method of claim 6, wherein said reagent mixture comprises a catalytic amount of ammonium molybdate.
12. The method of claim 6, wherein said heating is within a temperature range of 150 to 200°C.
13. The method of claim 12, wherein said heating is in the presence of solvent selected from the group comprising: nitrobenzene, diphenyl, diphenyl ether, mesitylene, anisole, phenetole, dichlorobenzene, trichlorobenzene and mixtures thereof.
14. The method of claim 4, wherein the benzoindolenine is liberated from the benzoindolenine salt using a base.
15. The method of claim 1, wherein said benzoindolenine is of formula (II):

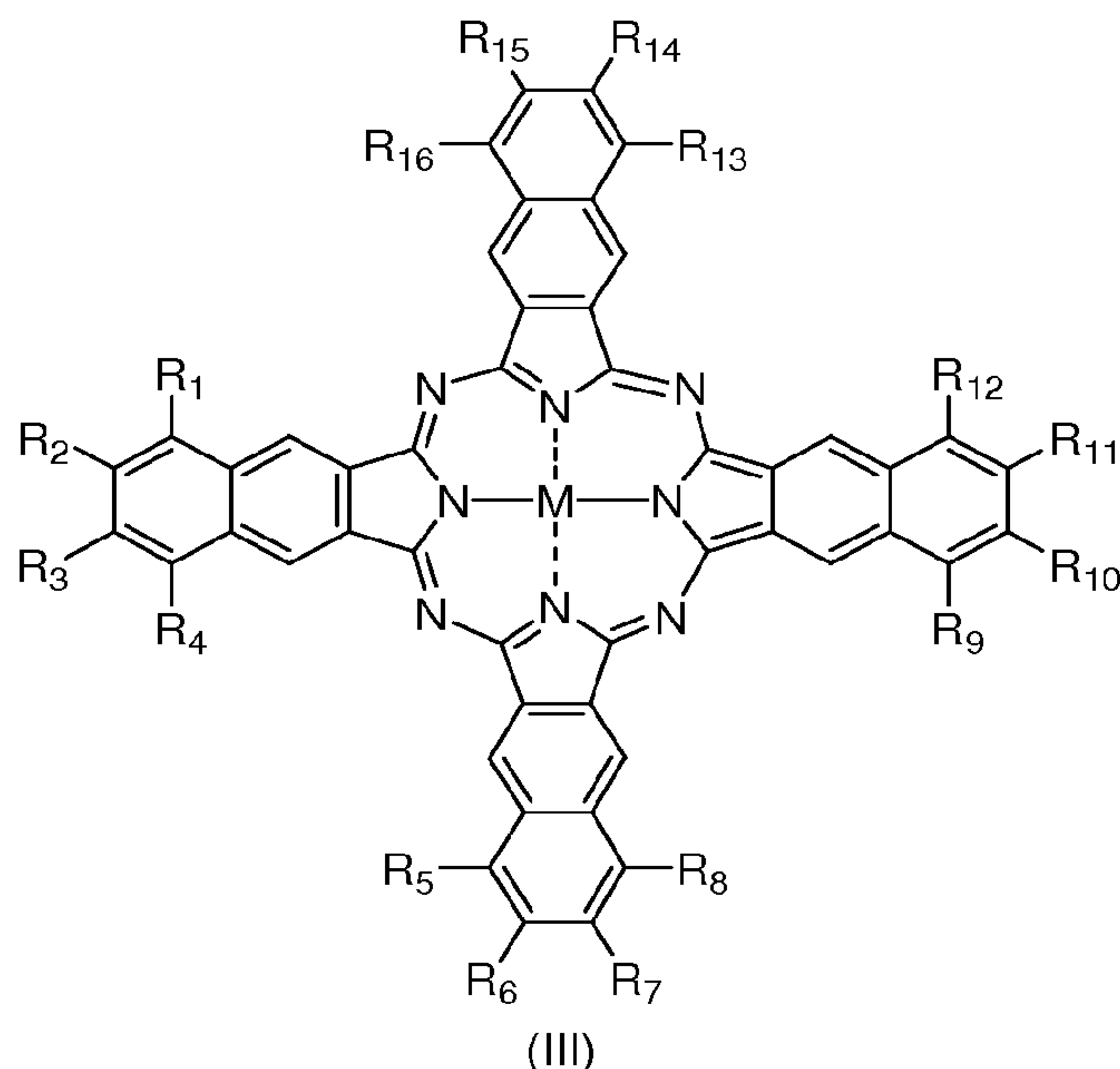


20 wherein:

R_1 , R_2 , R_3 and R_4 are each independently selected from hydrogen, hydroxyl, C_{1-20} alkyl, C_{1-20} alkoxy, amino, C_{1-20} alkylamino, di(C_{1-20} alkyl)amino, halogen, cyano, thiol, C_{1-20} alkylthio, nitro, C_{1-20} alkylcarboxy, C_{1-20} alkylcarbonyl, C_{1-20} alkoxy carbonyl, C_{1-20} alkylcarbonyloxy, C_{1-20} alkylcarbonylamino, C_{5-20} aryl, C_{5-20} arylalkyl, C_{5-20} aryloxy, C_{5-20} arylalkoxy, C_{5-20} heteroaryl, C_{5-20} heteroaryloxy, C_{5-20} heteroarylalkoxy or C_{5-20} heteroarylalkyl.

16. The method of claim 1, wherein said naphthalocyanine is of formula (III):

17



wherein:

- $R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{14}, R_{15}$ and R_{16} are each independently selected from hydrogen, hydroxyl, C_{1-20} alkyl, C_{1-20} alkoxy, amino, C_{1-20} alkylamino, di(C_{1-20} alkyl)amino, halogen, cyano, thiol, C_{1-20} alkylthio, nitro, C_{1-20} alkylcarboxy, C_{1-20} alkylcarbonyl, C_{1-20} alkoxy carbonyl, C_{1-20} alkylcarbonyloxy, C_{1-20} alkylcarbonylamino, C_{5-20} aryl, C_{5-20} arylalkyl, C_{5-20} aryloxy, C_{5-20} arylalkoxy, C_{5-20} heteroaryl, C_{5-20} heteroaryloxy, C_{5-20} heteroarylalkoxy or C_{5-20} heteroarylalkyl;
- M is absent or selected from $Si(A^1)(A^2)$, $Ge(A^1)(A^2)$, $Ga(A^1)$, Mg , $Al(A^1)$, TiO , $Ti(A^1)(A^2)$, ZrO , $Zr(A^1)(A^2)$, VO , $V(A^1)(A^2)$, Mn , $Mn(A^1)$, Fe , $Fe(A^1)$, Co , Ni , Cu , Zn , Sn , $Sn(A^1)(A^2)$, Pb , $Pb(A^1)(A^2)$, Pd and Pt ;
- A^1 and A^2 are axial ligands, which may be the same or different, and are selected from $-OH$, halogen or $-OR^q$;
- R^q is selected from C_{1-16} alkyl, C_{5-20} aryl, C_{5-20} arylalkyl, C_{1-20} alkylcarbonyl, C_{1-20} alkoxy carbonyl or $Si(R^x)(R^y)(R^z)$; and
- R^x, R^y and R^z may be the same or different and are selected from C_{1-20} alkyl, C_{5-20} aryl, C_{5-20} arylalkyl, C_{1-20} alkoxy, C_{5-20} aryloxy or C_{5-20} arylalkoxy;

17. The method of claim 16, wherein $R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{14}, R_{15}$ and R_{16} are all hydrogen.

18. The method of claim 16, wherein M is $Ga(A^1)$.

19. The method of claim 1, wherein step (iii) comprises heating said benzoindolenine in the presence of a metal compound.

20. The method of claim 1, wherein said method further comprises the step of:
(iv) sulfonating said naphthalocyanine.

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FIG. 1

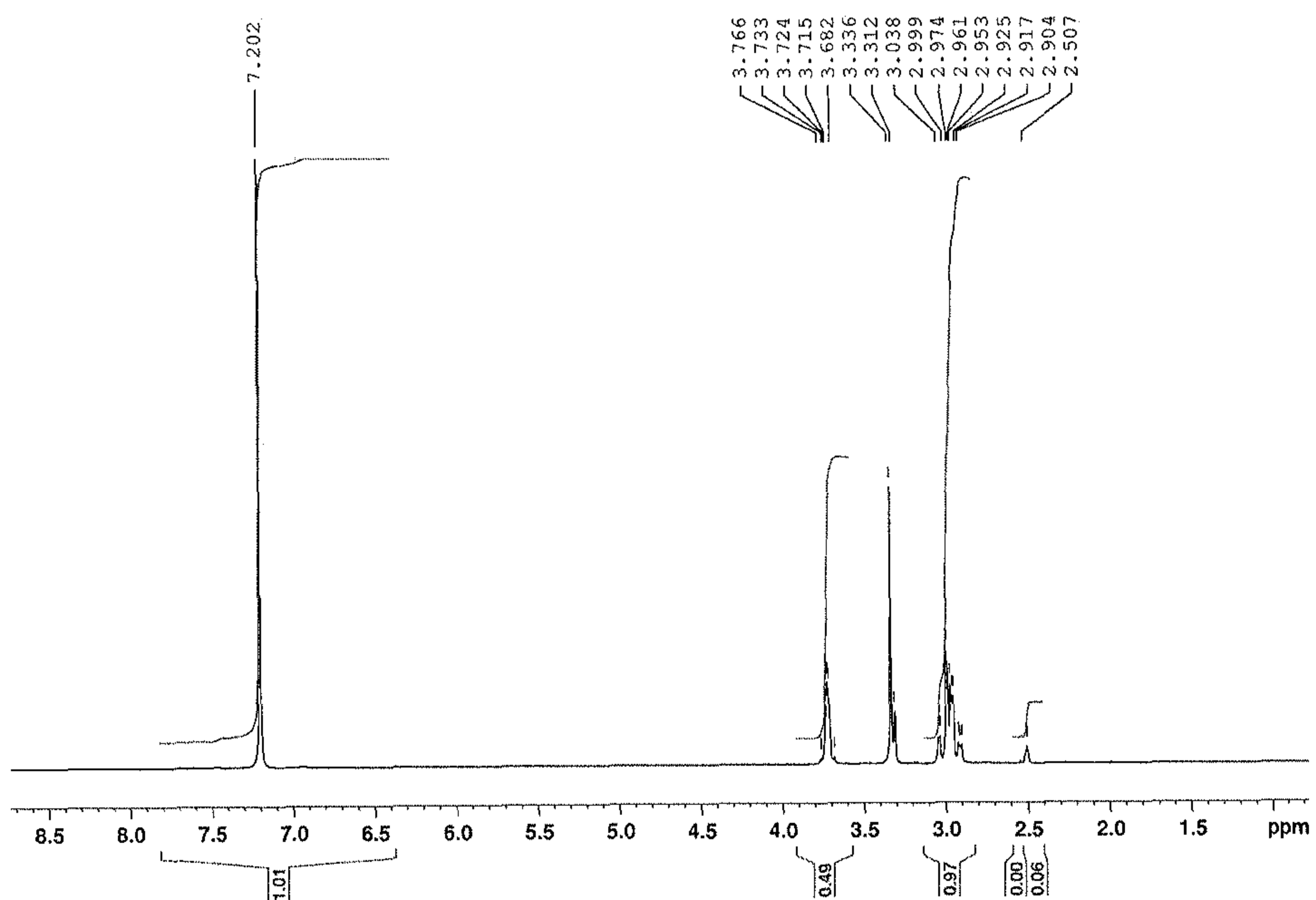


FIG. 2

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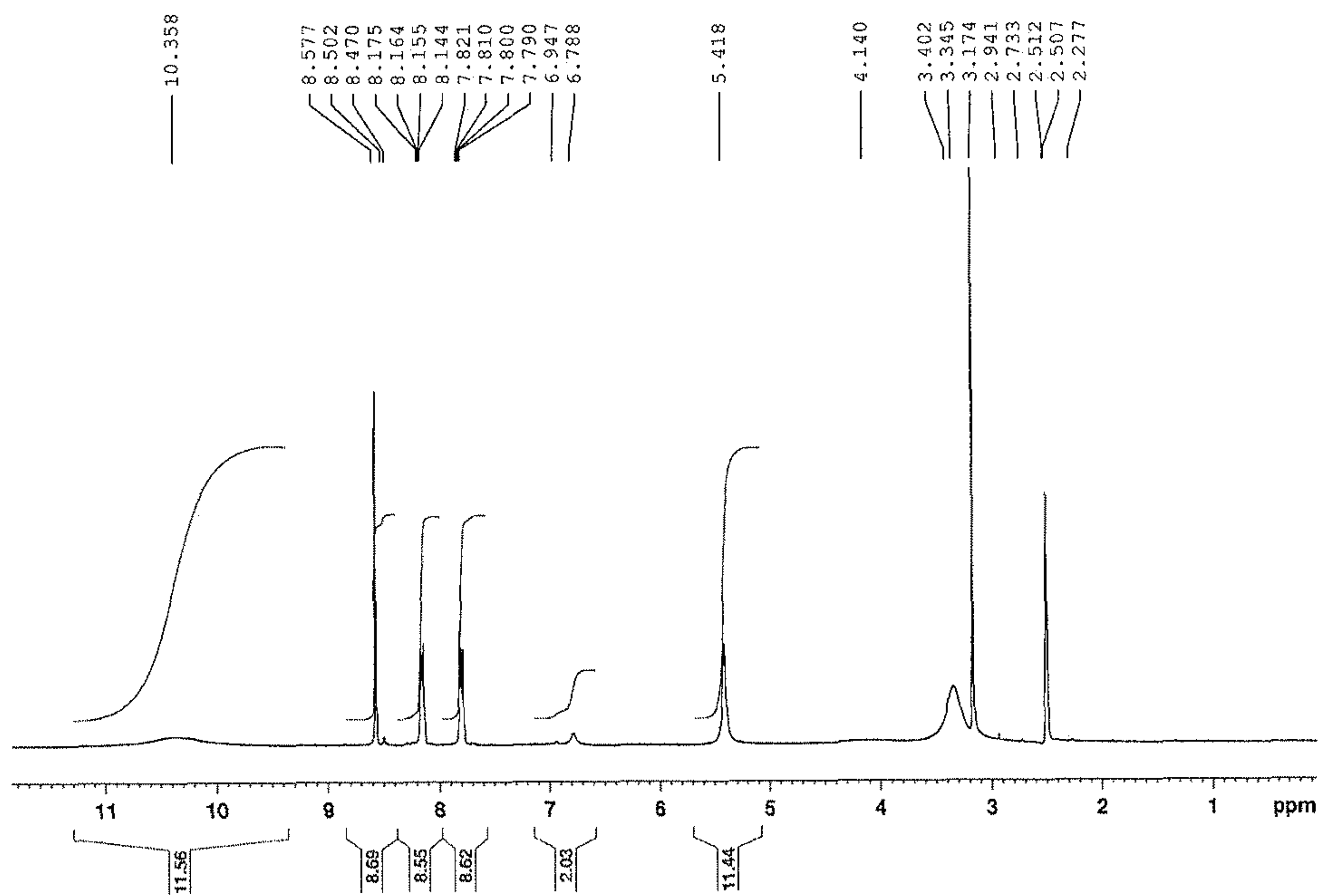


FIG. 3

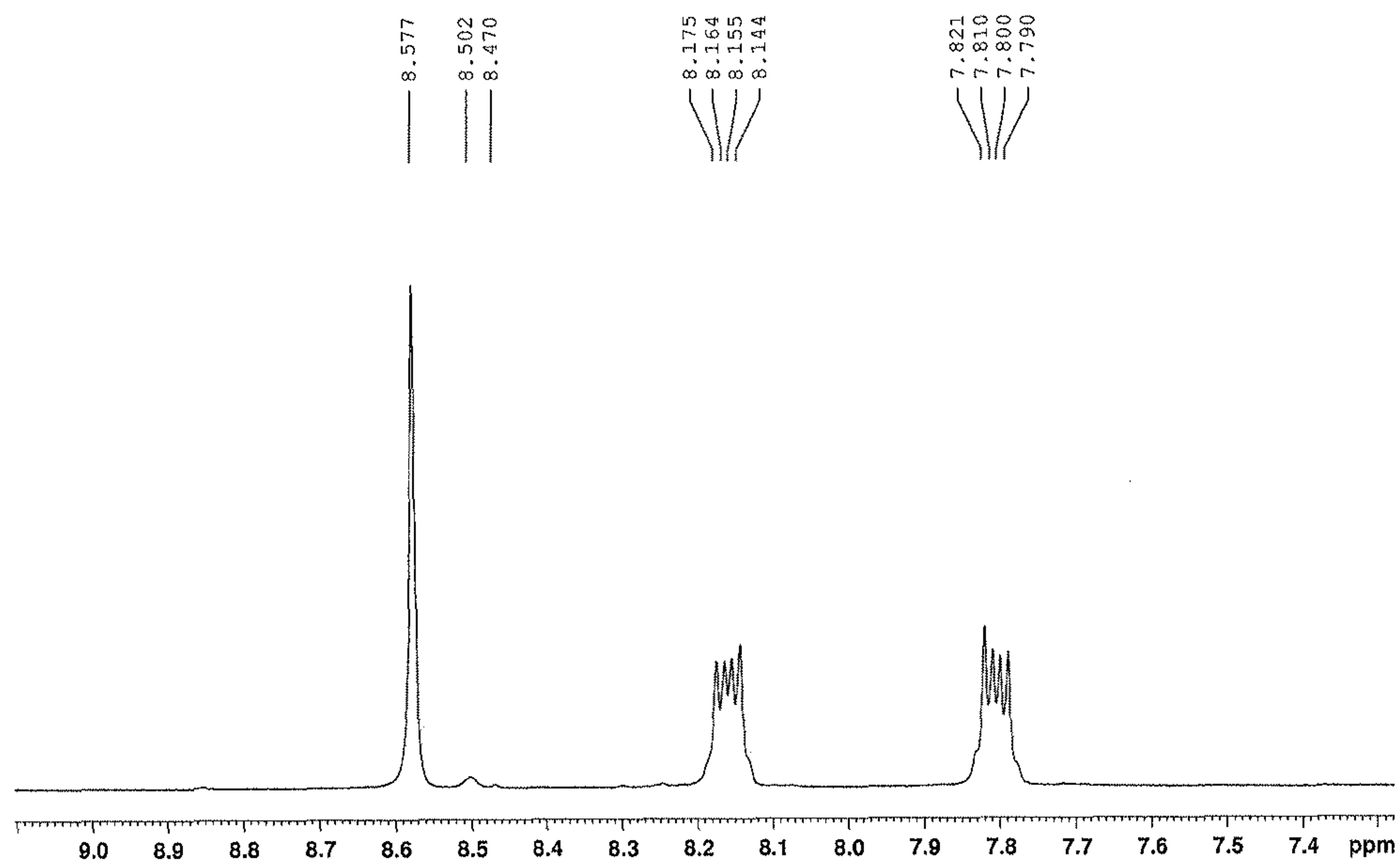


FIG. 4

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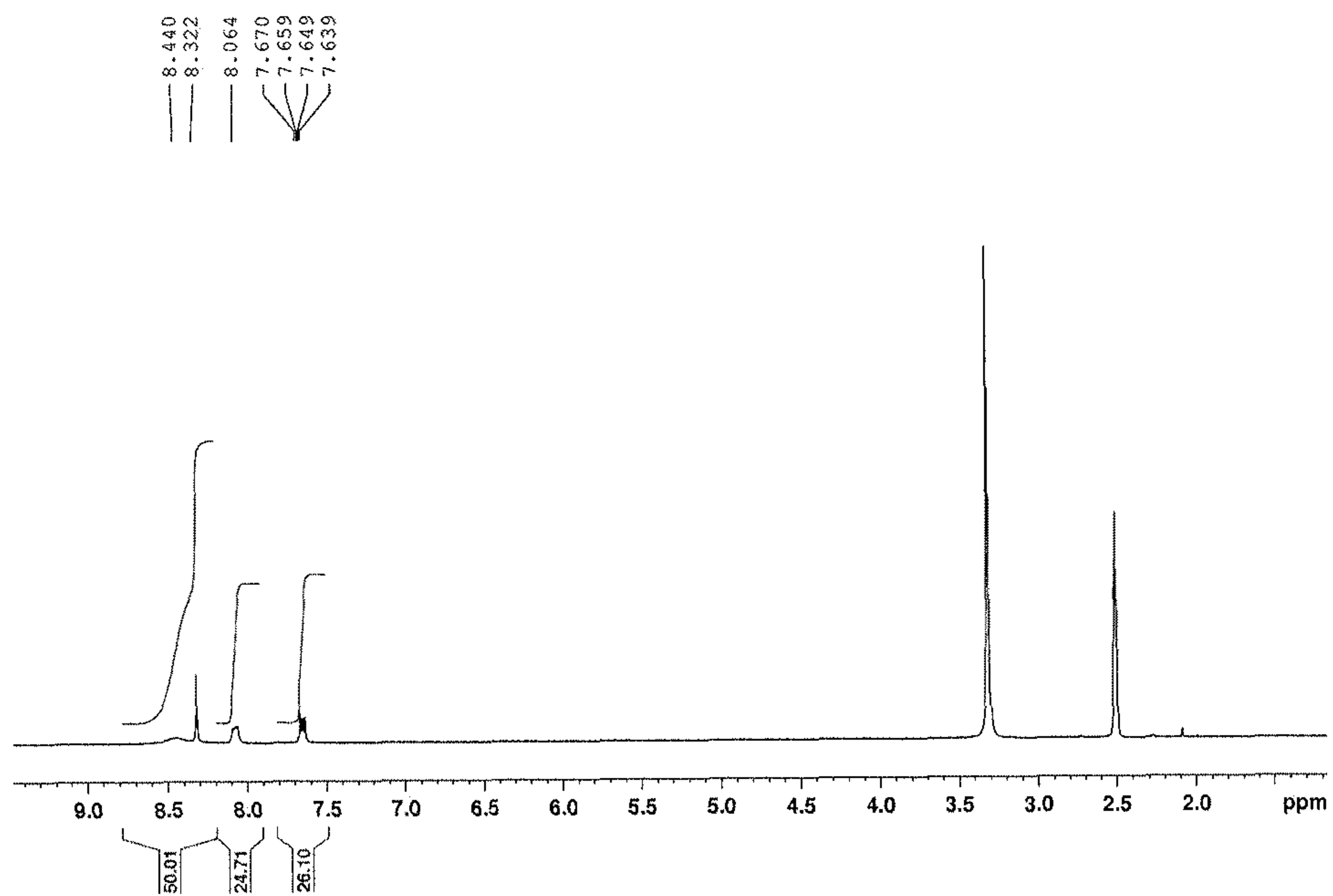


FIG. 5

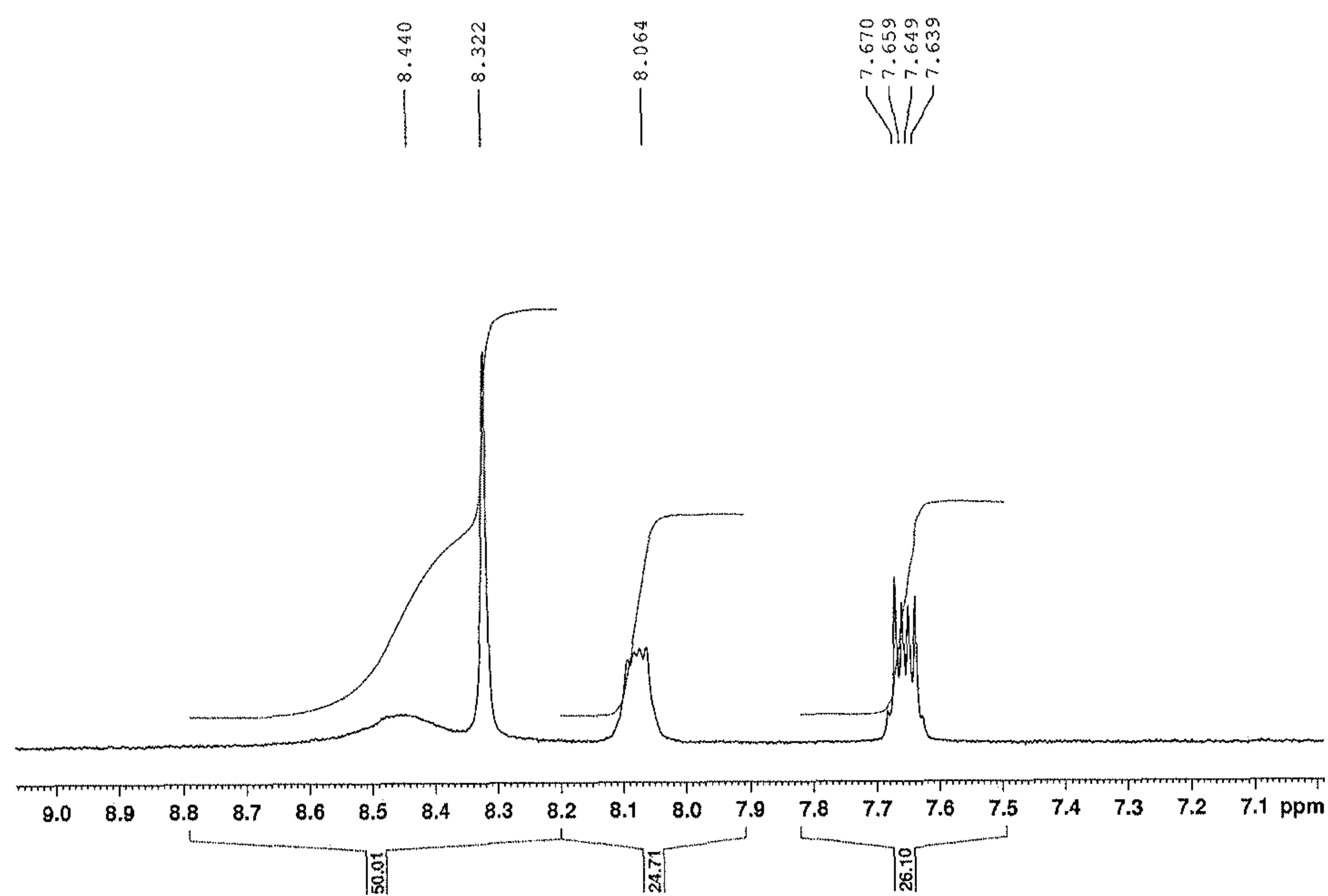


FIG. 6

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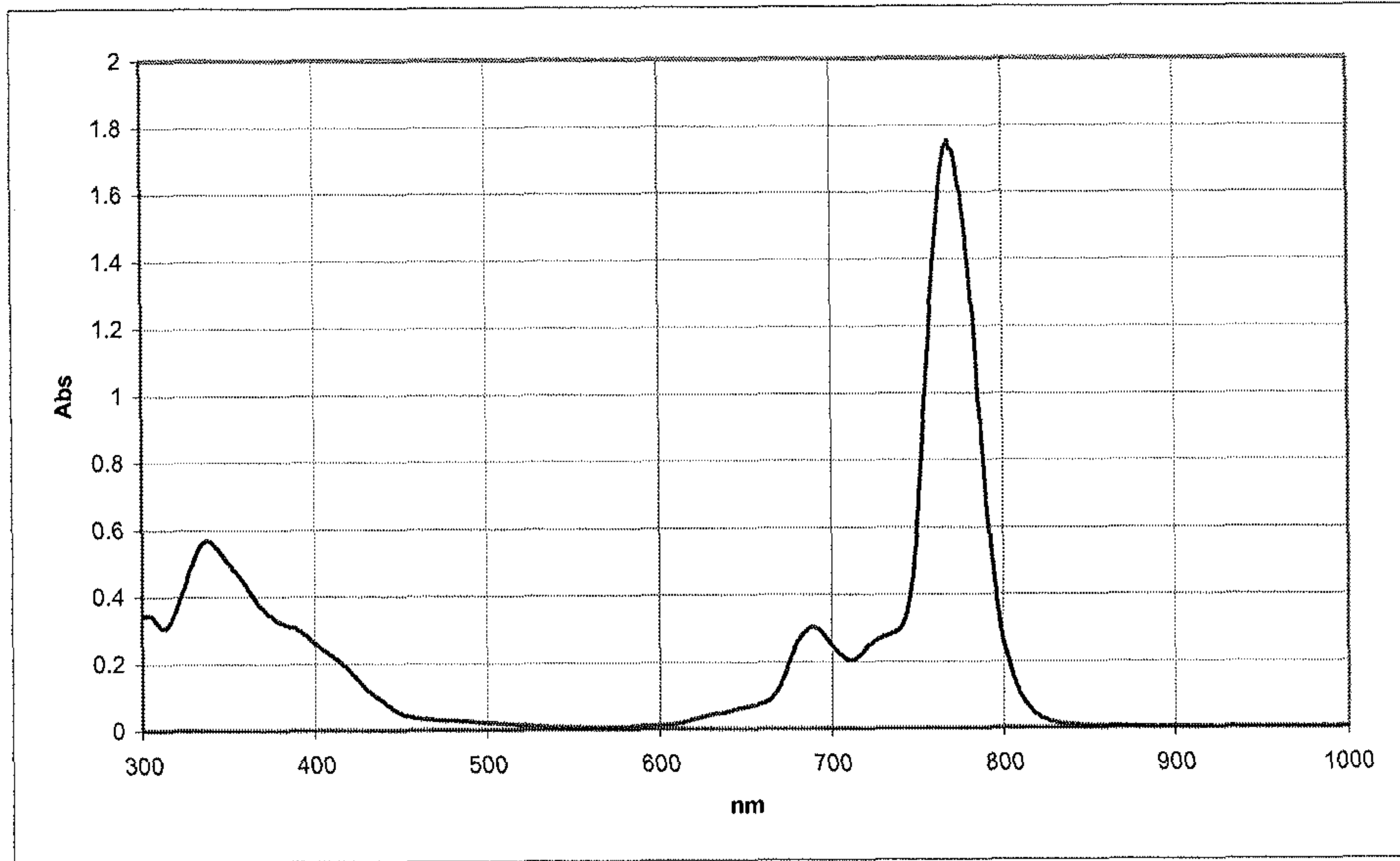


FIG. 7