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NOTICE OF ENTITLEMENT

(To be filed before acceptance)

We, **ASULAB S.A.** of Faubourg du Lac 6, CH-2501 Bienne, Switzerland, being the applicant in respect of Application No. 12441/92 state the following:-

The person nominated for the grant of the patent has entitlement from the actual inventors by assignment.

The person nominated for the grant of the patent is the applicant of the application listed in the declaration under Article 8 of the PCT.

The basic application is the first application made in a Convention country in respect of the invention.

ASULAB S.A.

By our Patent Attorneys,
WATERMARK PATENT & TRADEMARK ATTORNEYS

.....

Ian A. Scott

Registered Patent Attorney

30 June, 1994.

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(54) Title
MONO, BIS OR TRIS (2,2'-SUBSTITUTED BIPYRIDINE) COMPLEXES OF A METAL SELECTED AMONGST IRON, RUTHENIUM, OSMIUM OR VANADIUM AND PREPARATION METHODS THEREOF

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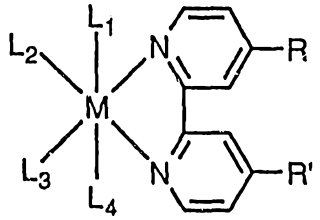
(57) Claim

1. A mono, bis or tris (4,4' substituted 2,2'-bipyridine) complex of a metal M having the following formula (I)



(I)

in which M represents osmium, R and R' being the same or different and at least one of which represents an electron donor group, selected from a hydroxy, methoxy, aryloxy group or an amino or dialkylamino group and L_1, L_2, L_3 and L_4 are taken in pairs to form two bidentate ligands, said bidentate ligands forming together with the 4,4'-substituted 2,2'-bipyridine moiety a coordination complex with the metal M.

20. A mediator for amperometric sensor wherein it is a complex according to any one of Claims 1 to 18.

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(54) Title: MONO, BIS OR TRIS (2,2'-SUBSTITUTED BIPYRIDINE) COMPLEXES OF A METAL SELECTED AMONGST IRON, RUTHENIUM, OSMIUM OR VANADIUM AND PREPARATION METHODS THEREOF

(54) Titre: COMPLEXES MONO, BIS OU TRIS (2,2'-BIPYRIDINE SUBSTITUEE) D'UN METAL CHOISI PARMI LE FER, LE RUTHENIUM, L'OSMIUM OU LE VANADIUM ET LEURS PROCEDES DE PREPARATION

(57) Abstract

The present invention relates to a new family of mono, bis or tris (2,2'-substituted bipyridine) complexes of a metal selected amongst iron, ruthenium, osmium or vanadium, the bipyridine being substituted by at least one electron donor group. According to the invention, said electron donor group is selected amongst a hydroxy group, an alkoxy group, an aryloxy group or a primary, secondary or tertiary amine group. The invention also relates to the method for the preparation of such complexes.

(57) Abrégé

La présente invention concerne une nouvelle famille de complexes mono, bis ou tris (2,2'-bipyridine substituée) d'un métal choisi parmi le fer, le ruthénium, l'osmium ou le vanadium, la bipyridine étant substituée par au moins un groupe donneur d'électrons. Selon l'invention ce groupe donneur d'électrons est choisi parmi un groupe hydroxy, un groupe alkoxy, un groupe aryloxy ou un groupe amine primaire, secondaire ou tertiaire. L'invention concerne également les procédés de préparation de ces complexes.

MONO, BIS OR TRIS(SUBSTITUTED 2,2'-BIPYRIDINE) IRON, RUTHENIUM, OSMIUM OR VANADIUM COMPLEXES AND THEIR METHODS OF PREPARATION

The instant invention relates to a new family of mono, bis or tris(substituted 2,2'-bipyridine) iron, ruthenium, osmium or vanadium complexes, the bipyridine being substituted by at least one electron donor group. This invention also relates to methods for the preparation of these complexes.

Determination of the concentration of certain components and especially of glucose in biological fluids has been considerably improved by the use of amperometric sensors using an electrode coated with a mediator and with an enzyme specific to said component, for example glucose oxidase for the detection of glucose. These sensors thus make it possible to measure the transfer of electrons passing between the enzyme and the electrode by the intermediary of the mediator, this electron transfer being proportional to the amount of component present in the sample of the biological fluid to be tested.

The quality of these sensors, i.e. their accuracy, the reproducibility of the results given by several sensors of the same series, their reliability and the speed of their response time largely depends upon the mediator used.



Mediators known to date, for example from US patent 4,545,382 of Genetics International, include polyviologen, chloranil, fluoranil or ferrocene.

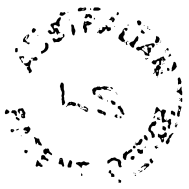
These mediators have, however, a certain number of disadvantages.

Because they do not transfer the electrons between the enzyme and the electrode sufficiently quickly, the response time of the sensor is rather long. In addition, some of these mediators, such as ferrocene, are relatively volatile or unstable, particularly when exposed to light and the sensors have to be stored under rather strict lighting and temperature conditions. In addition some mediators, especially ferrocene, decompose in water by hydrolysis which is a disadvantage when the sensors are used in blood.

Finally, oxygen enters into competition with some of these mediators and the results of glucose concentration measurements vary according to the amount of oxygen present in the blood. This can be a disadvantage depending on whether venous or arterial blood is being examined.

It was consequently desirable to seek and prepare mediators that are fast, stable and do not have interference problems with oxygen.

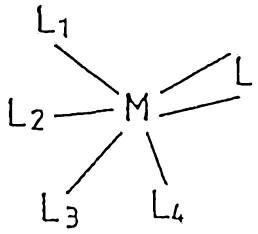
This search for mediators has led to the preparation of a new family of mono, bis or tris(substituted 2,2'-bipyridine) complexes of iron, ruthenium, osmium or vanadium, the bipyridine being substituted by at least one electron donor group.



This new family of complexes is not only of theoretical interest, but also above all because of these good mediator properties and the many other practical applications which it could have.

The invention will be better understood from a study of the following description of the family of complexes and of various embodiments of the processes for preparing these complexes.

The new family of mono, bis or tris(substituted 2,2'-bipyridine) complexes of a metal M has the following general formula (I):



(I)

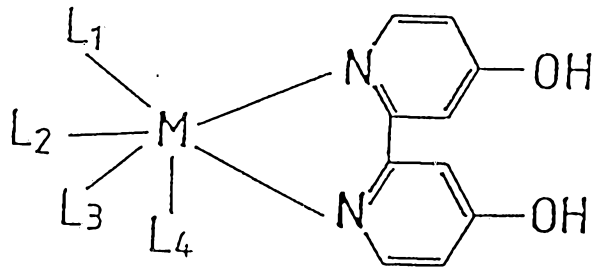
in which M is iron, osmium, ruthenium or vanadium.

L represents a bipyridine substituted by at least one electron donor group, conferring on the complex the oxidation-reduction properties desirable for a mediator. This electron donor group is preferably a hydroxy, alkoxy or aryloxy group or a primary, secondary or tertiary amine group.

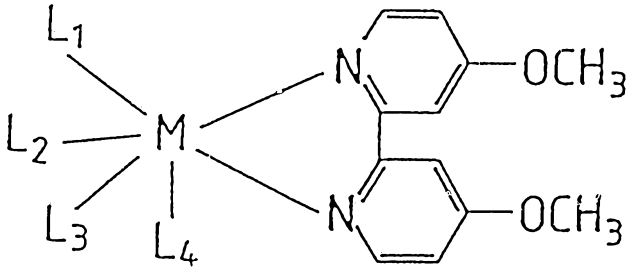
L_1, L_2, L_3, L_4 are ligands which together with L form a coordination complex with iron, osmium, ruthenium or vanadium.

It will also be noted that in these complexes, the ligand L preferably represents a bipyridine disubstituted in the

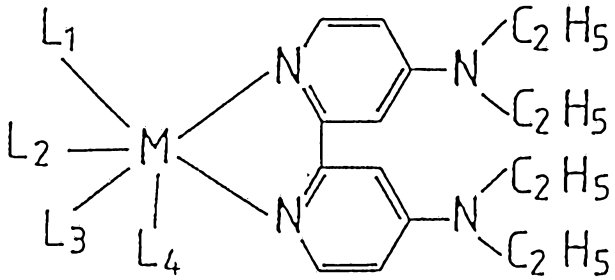
4,4'- positions and more particularly 4,4'-dihydroxy-2,2'-bipyridine, 4,4'-dimethoxy-2,2'-bipyridine or 4,4'-bis(N,N-ethyl amino)-2,2'-bipyridine also known as 4,4'-bis(N,N-diethylamino)-2,2'-bipyridine, the complexes then having the following general formulae referenced (II), (III) and (IV) respectively:



(II)



(III)



(IV)

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The ligands L_1, L_2, L_3 and L_4 are mono-, di-, ter- or tetradentate and may be combined in the following manner:

- either L_1, L_2, L_3 and L_4 each represents a monodentate ligand and are wholly or partially the same or different from one another,
- or L_1 and L_2 together are a bidentate ligand and L_3 and L_4 are the same or different and each represents a monodentate ligand,
- or L_1 and L_2 on the one hand and L_3 and L_4 on the other hand form respectively a bidentate ligand,
- or L_1 represents a monodentate ligand and L_2, L_3 and L_4 together form a terdentate ligand,
- or L_1, L_2, L_3 and L_4 together form a tetradentate ligand.

Monodentate ligands that can be used include: CN^-, Cl^-, Br^-, I^-, SCN^-, H_2O, NH_3, triphenylphosphine, trialkylphosphines, primary, secondary or tertiary amines, pyridine or pyridines substituted by Cl, NH_2, NO_2 or by an alkyl group.

Bidentate ligands that may be used include: ethylenediamine, 1,2 bis(2-pyridyl)ethane, oxalic acid $O^-CO-CO-O^-$, acetylacetone $CH_3-CO-CH_2-CO-CH_3$, glycine $NH_2-CH_2-COO^-$ and, preferably, a bipyridine or phenanthroline disubstituted by an R_1 group and an R_2 group, R_1 and R_2 being the same or different and each representing hydrogen, NO_2, Cl, an alkyl group, an aryl group, an OH group, an alkoxy group, an aryloxy group or a primary, secondary or tertiary amine group.

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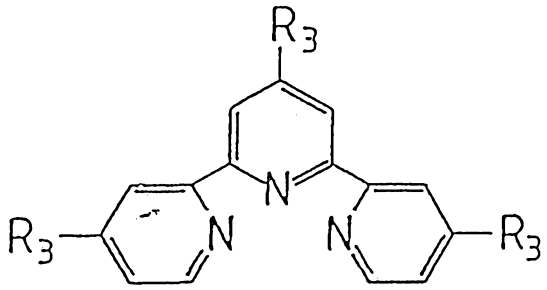
The terdentate ligand preferably used is terpyridine of the general formula (V):

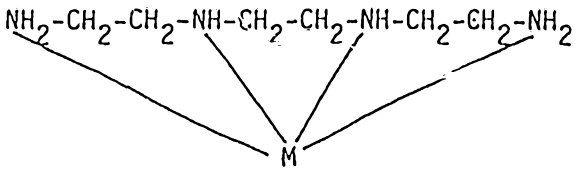


(V)

in which R_3 represents hydrogen or an alkyl group.

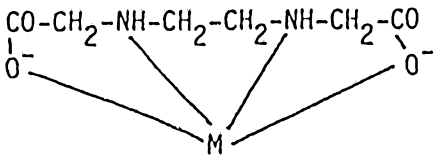
The terdentate ligand preferably used is

- triethylenetetraamine:



shown in the above diagram in coordination with the metal M, and

- ethylenediaminediacetic acid



also shown in coordination with the metal M.

When L_1 and L_2 on the one hand and L_3 and L_4 on the other hand form respectively a bidentate ligand and when these two bidentate ligands are the same as the ligand L, a tris complex (ligand L) is obtained of a metal M which is iron, ruthenium, osmium or vanadium.



The preferred tris (ligand L) complexes of the present invention are:

- tris(4,4'-dihydroxy-2,2'-bipyridine) complexes of the metal M, and
- tris(4,4'-dimethoxy-2,2'-bipyridine) complexes of the metal M, and
- tris(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine) complexes of the metal M.

When L_1 and L_2 together form a first bidentate ligand and when L_3 and L_4 together form a second bidentate ligand and when in addition only the first bidentate ligand is identical to the ligand L, a bis (ligand L) complex of the metal M is obtained, M being as defined above.

The preferred bis (ligand L) complexes of the instant invention are:

- bis(4,4'-dihydroxy-2,2'-bipyridine)mono(2,2'-bipyridine) complexes of the metal M,
- bis(4,4'-dihydroxy-2,2'-bipyridine)mono(4,4'-dimethoxy- 2,2'-bipyridine) complexes of the metal M,
- bis(4,4'-dihydroxy-2,2'-bipyridine)mono(4,4'-dimethyl- 2,2'-bipyridine) complexes of the metal M,
- bis(4,4'-dihydroxy-2,2'-bipyridine)mono(4-alkyl-2,2'-bipyridine) complexes of the metal M,
- bis(4,4'-dihydroxy-2,2'-bipyridine)mono(4,4'-dialkyl-2,2'-bipyridine) complexes of the metal M,
- bis(4,4'-dihydroxy-2,2'-bipyridine)mono(4,7-dihydroxy-1,10phenanthroline) complexes of the metal M,

- bis(4,4'-dihydroxy-2,2'-bipyridine)mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine) complexes of the metal M,

- bis(4,4'-dimethoxy-2,2'-bipyridine)mono(2,2'-bipyridine complexes of the metal M,

- bis(4,4'-dimethoxy-2,2'-bipyridine)mono(4,4'-dimethyl-2,2'-bipyridine) complexes of the metal M,

- bis(4,4'-dimethoxy-2,2'-bipyridine)mono(4-alkyl-2,2'-bipyridine) complexes of the metal M,

- bis(4,4'-dimethoxy-2,2'-bipyridine)mono(4,4'-dialkyl-2,2'-bipyridine) complexes of the metal M,

- bis(4,4'-dimethoxy-2,2'-bipyridine)mono(4,7-dihydroxy-1,10-phenanthroline) complexes of the metal M,

- bis(4,4'-dimethoxy-2,2'-bipyridine)mono(4,4'-dihydroxy-2,2'-bipyridine) complexes of the metal M,

- bis(4,4'-dimethoxy-2,2'-bipyridine)mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine) complexes of the metal M,

- bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine) mono-(2,2'-bipyridine) complexes of the metal M,

- bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine mono(4,4'-dimethoxy-2,2'-bipyridine) complexes of the metal M,

- bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine mono(4,4'-dimethyl-2,2'-bipyridine) complexes of the metal M,

- bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine mono(4-alkyl-2,2'-bipyridine) complexes of the metal M,

- bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine mono(4,4'-dialkyl-2,2'-bipyridine) complexes of the metal M,
- bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine mono(4,4'-dihydroxy-2,2'-bipyridine) complexes of the metal M,
- bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine mono(4,7-dihydroxy-1,10-phenanthroline) complexes of the metal M.

When L_1 and L_2 together form a first bidentate ligand and when L_3 and L_4 together form a second bidentate ligand and when in addition this first and this second ligand differ from the ligand L, a mono (ligand L) complex of a metal M which is iron, ruthenium, osmium or vanadium is obtained.

When this first ligand (L_1, L_2) and this second ligand (L_3, L_4) are identical, the preferred mono (ligand L) complexes of the instant invention are the following:

- mono(4,4'-dihydroxy-2,2'-bipyridine)bis(4,4'-dimethyl-2,2'-bipyridine) complexes of the metal M,
- mono(4,4'-dihydroxy-2,2'-bipyridine)bis(2,2'-bipyridine) complexes of the metal M,
- mono(4,4'-dihydroxy-2,2'-bipyridine)bis(4-alkyl-2,2'-bipyridine) complexes of the metal M,
- mono(4,4'-dihydroxy-2,2'-bipyridine)bis(4,7-dihydroxy-1,10-phenanthroline) complexes of the metal M,
- mono(4,4'-dimethoxy-2,2'-bipyridine)bis(4,4'-dimethyl-2,2'-bipyridine) complexes of the metal M,

- mono(4,4'-dimethoxy-2,2'-bipyridine)bis(2,2'-bipyridine) complexes of the metal M,

- mono(4,4'-dimethoxy-2,2'-bipyridine)bis(4-alkyl-2,2'-bipyridine)complexes of the metal M,

- mono(4,4'-dimethoxy-2,2'-bipyridine)bis(4,7-dihydroxy-1,10-phenanthroline) complexes of the metal M,

- mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)bis(4,4'-dimethyl-2,2'-bipyridine) complexes of the metal M,

- mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)bis(2,2'-bipyridine) complexes of the metal M,

- mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)bis(4-alkyl-2,2'-bipyridine) complexes of the metal M,

- mono(4,4'-bis(N,N-ethylamino)2,2'-bipyridine)bis(4,7-dihydroxy-1,10-phenanthroline) complexes of the metal M.

When said first ligand (L_1, L_2) and said second ligand (L_3, L_4) are different, the preferred mono (ligand L) complexes are the following:

- mono(4,4'-dimethoxy-2,2'-bipyridine)mono(4,4'-dihydroxy-2,2'-bipyridine)mono(4,4'-dimethyl2,2'-bipyridine) complexes of the metal M.

The instant invention also provides processes for the preparation of the above-described complexes.

The invention relates in particular to a process for the preparation of a tris (ligand L) complex of a metal M which is iron, ruthenium, osmium or vanadium. The ligand L is a bidentate ligand which is 4,4'-dimethoxy-2,2'-bipyridine,

4,4'- dihydroxy-2,2'-bipyridine or 4,4'-bis(N,N-ethylamino)2-2'- bipyridine.

This process generally comprises:

- reacting a soluble salt of the metal M with a substantially stoichiometric amount of a ligand A in the presence of solvents suitable for dissolving this ligand, and then in

- refluxing this solution under a nitrogen atmosphere at atmospheric pressure and at a temperature close to the boiling point of these solvents.

In the majority of cases, the ligand A is identical to the ligand L or is sufficiently similar thereto to transform into this ligand L during the reaction. The ligand A can, for example, be of the same type as the ligand L, but be differently substituted. This is the case in example 1, where one starts with a bipyridine disubstituted by two methoxy groups to obtain a bipyridine disubstituted by two hydroxy groups. In Example 1, as well as in Examples 5 and 11 described hereinabove 4,4'-dimethoxy-2,2'-bipyridine is used to obtain the complexes with 4,4'-dihydroxy-2,2'-bipyridine since this latter is not commercially available in view of the difficulties and costs of manufacture.

The nature of the soluble salt of the metal M varies as a function of the latter. Depending on whether the metal M is iron, ruthenium, osmium or vanadium, the soluble salts are $FeCl_2$, K_2OsCl_6, $RuCl_3$ or VCl_3 respectively.



The invention primarily relates to a process for the preparation of a tris(4,4-dihydroxy-2,2'-bipyridine) complex of a metal M which is iron, ruthenium, osmium or vanadium.

This process generally comprises:

- reacting a soluble salt of the metal M, M being as defined above, with a substantially stoichiometric amount of 4,4'-dimethoxy-2,2'-bipyridine in the presence of ethylene glycol, and then
- refluxing this solution under a nitrogen atmosphere at atmospheric pressure and at a temperature of between 190 and 200°C, preferably 195°C.

The soluble salts of the metal M are identical to those described above.

The choice of the solvent used (ethylene glycol) makes it possible to work at elevated temperatures (about 190 to 200°C) and to only cleave the bond between OCH_3 and the bipyridine without any other chemical changes occurring.

Once the OCH_3 bond is cleaved, the OH groups are then able to form to yield a tris(4,4'-dihydroxy-2,2'-bipyridine) complex of the metal M.

A specific example for obtaining one of these complexes is given below.

Example 1

Preparation of the complex tris(4,4'-dihydroxy-2,2'-bipyridine) osmium

0.100 g (0.21 mmol) of K_2OsCl_6 are dissolved in 10 ml ethylene glycol and 0.144 g (0.67 mmol) of 4,4'-dimethoxy-2,2'-bipyridine are added. The solution is refluxed for at least 24 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between about 190 and 200°C, preferably 195°C. A brown colour appears. After leaving the solution to cool to room temperature it is concentrated to half its original volume. The product is precipitated as its trifluoromethanesulfonate form by adding trifluoromethane sulfonic acid to the ethylene glycol solution.

The complex obtained is filtered, washed with a mixture (1:10 vol/vol) of acetone and diethyl ether and then dried under a high vacuum.

Tris(4,4'-dimethoxy-2,2'-bipyridine) osmium is obtained having the following physico-chemical properties:

- Elementary analysis

Formula: $C_{32}H_{24}N_6O_{12}F_6OsS_2$ (1.55 H_2O)

(measurements made with the trifluromethanesulfonate)

	Calculated	Found
C	35.56 %	35.75 %
H	2.53 %	3.02 %
N	7.78 %	7.10 %
H_2O	2.58 %	2.58 %

- Oxidation-reduction potential E° (normal potential)

When the complex is dissolved in an organic solvent such as acetonitrile in the presence of $LiCl_4$ 0.2 M, and a potentiodynamic measurement is carried out using a vitreous carbon electrode, one obtains E° = + 280 mV (in relation to a calomel reference electrode SCE).

In an aqueous solvent: PBS (phosphate buffer solution: NaCl 100 mM, NaH_2PO_4 10 mM, first adjusted to pH 7.4 then to pH 1 and then to pH 13) with a carbon electrode, one obtains:

- pH = 1 E° = + 150 mV (SCE)
- pH = 13 E° = - 1V (SCE)

- NMR

The sample dissolved in CD_2Cl_2 displays no OCH_3 peak at 4.1 ppm which indicates that these groups are completely hydrolysed to form OH groups. Aromatic proton peaks are observed between 6.8 ppm and 8 ppm in relation to a tetramethylsilane standard.



- Absorption spectrum data of UV and visible waves

wavelength λ max (nm)	extinction coefficient ε (M^{-1} cm^{-1})
239	13850
269	13300
300	12600
357	11500
385	10858
474	7430
512	6240
654	1475
712	1156

When the ligand L is 4,4'-dimethoxy-2,2'-bipyridine, the process for the preparation of the tris (ligand L) complex of metal M comprises:

- reacting a soluble salt of the metal M with a substantially stoichiometric amount of 4,4'-dimethoxy-2,2'-bipyridine in the presence of methanol, of DMF (dimethylformamide) and/or water, and then
- refluxing this solution under a nitrogen atmosphere at atmospheric pressure and at a temperature between about 70 and 80°C.

The choice of the solvents used (methanol, DMF and/or water) is important because it makes it possible, unlike in Example 1, to work at relatively low temperatures (about 70

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to 80°C) and thereby avoid cleavage of the bond between the OCH_3 group and the bipyridine. In addition, these solvents make it possible to reduce the metal M from a + 3 oxidation state to a + 2 state for ruthenium, from a + 4 state to a + 2 state for osmium and from a + 3 state to a + 2 state for vanadium. Iron does not change the oxidation state, being already in the + 2 oxidation state. Nonetheless it will be noted that for the vanadium it is necessary to use additional reagents to reach the desired 0 oxidation state

A specific example for obtaining one of these complexes is given below.

Example 2

Preparation of the complex tris(4,4'-dimethoxy-2,2'-bipyridine) osmium.

0.100 g (0.21 mmol) of K_2OsCl_6 is dissolved in a mixture of 5 ml of water, 5 ml of methanol and 5 ml of DMF. 0.144 g (0.67 mmol) of 4,4'-dimethoxy-2,2'-bipyridine are added to this solution and the mixture is refluxed for at least 60 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between about 70 and 80°C.

A brown colour appears. After cooling to the room temperature the solution is filtered and the solvent is completely eliminated by rotary evaporation. A minimum of ethanol is then added to dissolve the product and the

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solution is then filtered to remove the insoluble KCl. The product is then precipitated in the form of the trifluoromethanesulfonate by addition of dilute trifluoromethanesulfonic acid. The complex is then filtered, washed with a 1:10 vol/vol mixture of acetone and diethylether and then dried under a high vacuum.

A tris(4,4'-dimethoxy-2,2'-bipyridine) osmium complex is then formed with the following physico-chemical properties:

- Elementary analysis

Formula: $C_{38}H_{36}N_6O_{12}F_6OsS_2$ (1.11 H_2O)

(measurements made with the trifluromethanesulfonate)

	Calculated	Found
C	39.45 %	39.13 %
H	3.33 %	3.27 %
N	7.26 %	7.41 %
H_2O	1.73 %	1.73 %

- Oxidation-reduction potential E° (normal potential)

When the complex is dissolved in an organic solvent such as acetonitrile in the presence of $LiCl_4$ 0.2 M, and a potentiodynamic measurement is carried out using a vitreous carbon electrode, one obtains E° = + 325 mV in relation to a calomel reference electrode (SCE).

In an aqueous solvent: PBS (phosphate buffer solution: NaCl 100 mM, NaH_2PO_4 10 mM, first adjusted to pH 7.4) with a carbon electrode, one obtains E° = + 225 mV.

- NMR

The sample dissolved in CD_2Cl_2 displays a OCH_3 peak at 4.1 ppm and aromatic proton peaks between 6.8 ppm and 8.0 ppm in relation to a tetramethylsilane standard.

- Absorption spectrum data of UV and visible waves

wavelength λ max (nm)	extinction coefficient ε (M^{-1} cm^{-1})
228	80800
271	70800
333	22236
385	16012
397	15296
470	12564
510	11404
630	4820
696	4012

The general process for preparing a tris(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine) complex of a metal M which is iron, ruthenium, osmium or vanadium will now be described.

This process comprises:

- reacting a soluble salt of the metal M with a substantially stoichiometric amount of 4,4'-bis(N,N-ethylamino)-2,2'-bipyridine in the presence of ethylene glycol and then
- refluxing this solution under a nitrogen atmosphere at atmospheric pressure and at a temperature between about 190 and 200°C, preferably 195°C.

The soluble salt of the metal M is identical to those previously described.

A specific example for obtaining one of these complexes is given below.

Example 3

Preparation of the complex tris(N,N-ethylamino)-2,2'-bipyridine) osmium

0.100 g (0.21 mmol) of K_2OsCl_6 is dissolved in 10 ml of ethylene glycol and 0.193 g (0.64 mmol) of 4,4'-bis(N,N-ethylamino)-2,2'-bipyridine are added. This solution is refluxed for at least 10 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between about 190 and 200°C, preferably at 195°C. After allowing the solution to cool to room temperature it is filtered and the

solvent is concentrated to half its original volume. The product is precipitated in the form of the trifluoromethanesulfonate by adding trifluoromethanesulfonic acid.

The complex obtained is filtered, washed with a mixture (1:10 vol/vol) of acetone and diethylether and dried under a high vacuum.

The instant invention also relates to the preparation of the bis (ligand L) mono (ligand B) complex of a metal M which is iron, osmium, ruthenium or vanadium, the ligand L being 4,4'-dimethoxy-2,2'-bipyridine; 4,4'-dihydroxy-2,2'-bipyridine or 4,4'-bis(N,N-ethylamino)-2,2'-bipyridine) and the ligand B being a bidentate ligand such as those referred to at the beginning of the specification.

One embodiment of this complex (bis ligand L) Cl_2 of said metal M will now be described. It is, however, obvious that the bis (ligand L) Cl_2 complex of the metal M used in the preparation of the bis (ligand L) mono (ligand B) complex of the metal M does not necessarily have to be prepared as described herein.

The preparation of the bis (ligand L) Cl_2 complex of a metal M which is iron, osmium, ruthenium or vanadium, the ligand L being 4,4'-dimethoxy-2,2'-bipyridine or 4,4'-dihydroxy-2,2'-bipyridine generally comprises:

- reacting a soluble salt of the metal M (M being as described above) with a substantially stoichiometric amount of 4,4'-dimethoxy-2,2'-bipyridine in the presence of an

appropriate mixture of solvents, especially for example water and methanol in the case of the first ligand L and ethylene glycol in the second case, and then

- refluxing this solution under a nitrogen atmosphere at atmospheric pressure and for example at a temperature between 70 and 80°C if water and methanol is used or at a temperature between 190 and 200°C if ethylene glycol is used.

The preparation of this same complex when the ligand L is 4,4'-bis(N,N-ethylamino)-2,2'-bipyridine generally comprises:

- reacting a soluble salt of the metal M, M being as defined above, with a substantially stoichiometric amount of 4,4'-bis(N,N-ethylamino)-2,2'-bipyridine in the presence of DMF and then

- refluxing this solution under a nitrogen atmosphere at atmospheric pressure and at a temperature between 150 and 155°C.

In these two cases, the soluble salts of the metal M are those described earlier.

Three more specific examples of preparation are given below.



Example 4

Preparation of the complex bis(4,4'-dimethoxy-2,2'-bipyridine) osmium

0.100 g (0.21 mmol) of K_2OsCl_6 are dissolved in a mixture of 5 ml of water and 5 ml of methanol and 0.90 g (0.42 mmol) of 4,4'-dimethoxy-2,2'-bipyridine are added to the solution. The solution is refluxed for at least 2 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between 70 and 80°C. A dark violet colour appears. The solution is allowed to cool to room temperature and the solvent is completely removed by rotary evaporation. 10 ml of water are then added. The bis(4,4'-dimethoxy-2,2'-bipyridine) Cl_2 osmium complex is then isolated by filtration, washed with water and then with a mixture of acetone and diethylether (1:6 vol/vol) to eliminate traces of unreacted ligand. Finally, this complex is dried under a high vacuum.

The results of the elementary analysis are given below.

- Elementary analysis

Formula: $C_{24}H_{24}N_4O_4OsCl_2$

	Calculated	Found
C	41.56 %	42.02 %
H	3.49 %	3.73 %
N	8.08 %	8.45 %



Example 5

Preparation of a bis(4,4'-dihydroxy-2,2'-bipyridine) Cl_2 osmium complex

0.100 g (0.21-mmol) of K_2OsCl_6 are dissolved in a mixture of 2 ml of water and 10 ml of ethylene glycol and 0.090 g (0.42 mmol) of 4,4'-dimethoxy-2,2'-bipyridine are added to the solution. The solution is refluxed for at least 16 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between 190 and 200°C, preferably 195°C. A dark violet colour appears. The solution is cooled to room temperature and then concentrated by rotary evaporation. The product obtained is precipitated by addition of acetone. The precipitate is isolated by filtration, washed with acetone and ether and then dried under a high vacuum.

The bis(4,4'-dihydroxy-2,2'-bipyridine) Cl_2 osmium complex obtained in this manner takes the form of blue crystals. The yield is 80 to 90%.

In these two Examples 4 and 5, the choice of solvents and the reaction temperatures were governed by the same rationale as that previously referred to.

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Example 6

Preparation of the complex bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine Cl_2 osmium.

0.100 g (0.21-mmol) of K_2OsCl_6 are dissolved in 10 ml DMF and 0.125 g (0.42 mmol) of 4,4'-bis(N,N-ethylamino)2,2'-bipyridine are added to the solution.

The solution is refluxed for at least 4 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between 150 and 155°C. The solution is allowed to cool to the room temperature and the solvent is completely removed by rotary evaporation. 10 ml of cold water are added and the complex bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine) Cl_2 osmium (which is poorly soluble) is isolated by filtration. This complex is then washed with cold water and then with a mixture (1:6 vol/vol) of acetone and diethylether to remove trace of unreacted ligand and then dried under high vacuum.

The preparation of the bis (ligand L) mono (ligand B) complex of a metal M, previously referred to will now be described.

This process comprises:

- reacting a bis (ligand L) Cl_2 complex of said metal M with a substantially stoichiometric amount of the ligand B in the presence of suitable solvents to dissolve this complex and the ligand B and then

- refluxing the solution under a nitrogen atmosphere at atmospheric pressure and at a temperature around the boiling point of these solvents.

As previously mentioned, if the ligand B is 4,4'-dihydroxy-2,2'-bipyridine the chlorinated complex is preferably reacted with 4,4'-dimethoxy-2,2'-bipyridine because this is readily available on the market.

Three more specific embodiments will now be described.

Example 7

Preparation of the complex bis(4,4'-dimethoxy-2,2'-bipyridine) mono(4,4'-dimethyl-2,2'-bipyridine) osmium

0.05 g (0.07 mmol) of a bis(4,4'-dimethoxy-2,2'-bipyridine) osmium complex are reacted with 0.017 g (0.09 mmol) 4,4'-dimethyl-2,2'-bipyridine in the presence of a mixture of 10 ml of DMF (dimethylformamide), 10 ml water and 10 ml methanol. The mixture is refluxed for at least 40 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between 70 and 80°C. Finally, the reaction mixture is allowed to cool to the room temperature, is filtered and the solvent is completely removed by rotary evaporation. The product is then dissolved in a minimum of ethanol and precipitated in the form of the trifluoromethanesulfonate by adding trifluoromethanesulfonic acid. Finally, the precipitate is filtered, washed with a mixture of acetone and diethylether (1:6 vol/vol) and dried under high vacuum.

- Elementary analysis

Formula: $C_{38}H_{36}N_6O_{10}F_6OsS_2$ (measurements made with the trifluromethane-sulfonate)
($0.90\ H_2O$)

	Calculated	Found
C	40.71 %	41.03 %
H	3.40 %	3.46 %
N	7.5 %	7.58 %
F	10.17 %	10.24 %
H_2O	1.45 %	1.44 %

- Oxidation-reduction potential E° (normal potential)

When the complex is dissolved in an organic solvent such as acetonitrile in the presence of $LiClO_4$ 0.2 M and a potentiodynamic measurement is effected using a vitreous carbon electrode one obtains E° = + 450 mV (reference: calomel electrode SCE). In a phosphate buffer PBS (NaCl 100 mM, $NaH_2\ PO_4$ 10 mM adjusted to pH 7.4), with a vitreous carbon electrode one obtains E° = + 340 mV (reference: calomel electrode SCE).

- NMR

The sample dissolved in CD_2Cl_2 gives a peak for OCH_3 at 4.1 ppm and a peak for CH_3 at 2.65 ppm as well as

aromatic proton peaks between 6.8 ppm and 8.0 ppm in relation to a tetramethylsilane standard.

- Absorption spectrum data of the UV and visible waves

wavelength λ max (nm)	extinction coefficient ε (M^{-1} cm^{-1})
216	108000
290	62000
336	15520
378	14580
462	13528
494	13376
628	6920
674	6540

Example 8

Preparation of the complex bis(4,4'-dihydroxy-2,2'-bipyridine) mono(4,4'-dimethyl-2,2'-bipyridine) osmium.

0.05 g (0.07 mmol) of bis(4,4'-dihydroxy-2,2'-bipyridine) Cl_2 osmium complex is reacted with 0.017 g (0.09 mmol) of 4,4'-dimethyl-2,2'-bipyridine in 10 ml ethylene glycol, the mixture is refluxed for at least 4 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between 190 and 200°C, preferably 195°C. A brown

colour appears. The reaction mixture is cooled to room temperature and then the solvent is concentrated to half its original volume. The product obtained is precipitated in the form of the trifluoromethanesulfonate by addition of dilute trifluoromethanesulfonic acid to the ethylene glycol solution. The bis(4,4'-dihydroxy-2,2'-bipyridine) mono(4,4'-dimethyl-2,2'-bipyridine) osmium complex obtained is filtered, washed with a mixture of acetone and diethylether (1:10 vol/vol) and dried under a high vacuum.

Example 9

Preparation of the complex bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine) mono(4,4'-dimethyl-2,2'-bipyridine) osmium.

0.05 mg (0.058 mmol) of bis(4,4'-bis-(N,N ethylamino)-2,2'-bipyridine) Cl_2 osmium complex is reacted with 0.014 g (0.07 mmol) of 4,4'-dimethyl-2,2'-bipyridine in 10 ml ethylene glycol and this solution is then refluxed for at least 6 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between 190 and 200°C, preferably at 195°C. The reaction mixture is cooled to room temperature and then filtered and the solvent concentrated to half its original volume. The product obtained is precipitated in the form of the trifluoromethanesulfonate by adding trifluoromethanesulfonic acid. The precipitate is filtered, washed with a mixture (1:6 vol/vol) of acetone and diethylether then dried under high vacuum.

The processes of preparation that have just been described in Examples 7, 8 and 9 for osmium may be generalized to iron, ruthenium and vanadium.

The invention also relates to a process for the preparation of a-mono (ligand L) bis (ligand B) complex of a metal M which is iron, osmium, ruthenium or vanadium. As before, the ligand L is 4,4'-dimethoxy-2,2'-bipyridine; 4,4'-dihydroxy-2,2'- bipyridine or 4,4'-bis(N,N-ethylamino)-2,2'-bipyridine and the ligand B is one of the bidentate ligands referred to at the beginning of the specification.

This procedure generally comprises:

- reacting a bis (ligand B) Cl_2 complex of said metal M with a ligand A in the presence of appropriate solvents to dissolve this complex and the ligand A, the ligand A being chosen in such a way as to transform itself into ligand L during the reaction,
- in refluxing this solution under a nitrogen atmosphere at atmospheric pressure and at a temperature close to the boiling point of said solvents.

As has already been seen, the ligand A is generally identical to the ligand L or is of the same nature as this ligand with different substituents. Example 11 illustrates the latter case for example.

Three more specific embodiments are given below.



Example 10

Preparation of the complex mono(4,4'-dimethoxy-2,2'-bipyridine)bis4,4'-dimethyl-2,2'-bipyridine) osmium.

0.05 g (0.08 mmol) of a bis(4,4'-dimethyl-2,2'-bipyridine) Cl_2 osmium complex, the preparation of which is known per se, is reacted with 0.022 g (1.0 mmol) of 4,4'-dimethoxy-2,2'- bipyridine in a mixture of 10 ml of DMF (dimethylformamide), 10 ml of water and 10 mg of methanol. The solution is refluxed for at least 40 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between 70 and 80°C. The reaction mixture is cooled to the room temperature, filtered and the solvent is completely eliminated by rotary evaporation.

The product is dissolved in a minimum of ethanol and then precipitated in the form of the trifluoromethanesulfonate by addition of trifluoromethanesulfonic acid. The complex obtained in the form of a precipitate is filtered with a mixture of acetone and of diethylether (1:6 vol/vol) and then dried under a high vacuum.

This complex has the following physico-chemical properties:

- Oxidation-reduction E° potential (normal potential)

When the complex is dissolved in an organic solvent such as acetonitrile in the presence of a salt of $LiClO_4$ 0.2 M and

a potentiodynamic measurement is effected using a vitreous carbon electrode one obtains E° = + 500 mV (calomel reference electrode SCE).

In a phosphate buffer PBS (NaCl 100 mM, NaH_2PO_4 10 mM adjusted to pH 7.4) with a vitreous carbon electrode one obtains E° = + 390 mV (calomel reference electrode SCE).

- Absorption spectrum data of the UV and visible waves

wavelength λ max (nm)	extinction coefficient $\varepsilon(M^{-1}\ cm^{-1})$
222	70248
290	61806
340	13919
380	13884
452	12113
498	12119
624	4763
684	4061

Example 11

Preparation of the complex mono(4,4'-dihydroxy-2,2'-bipyridine)bis(4,4'-dimethyl-2,2'- bipyridine) osmium.

The process is similar to that described in Example 10 except that 0.05 g (0.08 mmol) of bis(4,4'-dimethyl-2,2'-bi-

pyridine) Cl_2 osmium complex is reacted with 0.0195 g (0.09 mmol) of 4,4'-dimethoxy-2,2'-bipyridine in 10 ml of ethylene glycol and that the mixture is refluxed under a nitrogen atmosphere for at least 16 hours at atmospheric pressure and at a temperature between 190 and 200°C, preferably 195°C.

Example 12

Preparation of the complex mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)-bis(4,4'-dimethyl-2,2'-bipyridine) osmium.

0.05 g (0.08 mmol) of a bis(4,4'-dimethyl-2,2'-bipyridine) Cl_2 osmium complex, the preparation of which is known per se, is reacted with 0.026 g (0.08 mmol) of 4,4'-bis(N,N-ethylamino) -2,2'-bipyridine in 10 ml of ethylene glycol. The solution is refluxed for at least 6 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between 190 and 200°C, preferably 195°C. The reaction mixture is cooled to the room temperature, filtered and the solvent is concentrated to half its original volume. The product is precipitated in the form of the trifluromethanesulfonate by addition of dilute trifluoromethanesulfonic acid. The precipitate obtained is filtered, washed with a mixture (1:6 vol/vol) of acetone and diethylether and then dried under a high vacuum.

The description given in Examples 10, 11 and 12 for osmium can be generalized to iron, ruthenium and vanadium.



In examples 1 to 3 and 7 to 12 the final product is isolated by addition of trifluoromethanesulfonic acid. Nonetheless it is obvious that other salts could be obtained by selecting the appropriate reagents. It would thus be possible to obtain hexafluorophosphates by addition of potassium hexafluorophosphate. In the case of osmium and the use of K_2OsCl_6 as starting substance, chlorides could be obtained by adding diethylether.

Example 13

Preparation of the complex
tris (4,4'-diamino-2,2' bipyridine) ruthenium

0,1 g (0,38mmol) of 4,4' diamino-2,2'-bipydidine is dissolved. This solution is refluxed at least 4 hours under a nitrogen atmosphere at atmospheric pressure and at a temperature between 190 and 200°C, preferably 195°C. After cooling to room temperature 5 ml of acetone and 20 ml of diethylether are added. Then the ether is separated and removed. 20 ml of ether are added anew and the processus is renewed until the complex precipitate. This complex is separated by filtration, washed with ether and dried under high vacuum.



- Oxidation-reduction potential E° (normal potential)

When the complex is dissolved in an organic solvent such as acetonitrile in the presence of $LiClO_4$ 0.2 M and a potentiodynamic measurement is effected using a vitreous carbon electrode one obtains E° = + 450 mV (reference: calomel electrode SEC). In a phosphate buffer PBS (NaCl 100 mM, NaH_2PO_4 10 mM adjusted to pH 7.4), with a vitreous carbon electrode one obtains E° = 170 mV (reference: calomel electrode SCE).

- Absorption spectrum date of the UV and visible waves

wavelength λ max (nm)	extinction coefficient $\varepsilon(M^{-1}\ cm^{-1})$
354	17655
394	11988
472	8064
514	9444

Example 14

Preparation of the complex
tris (4,4'-diamino-2,2'-bipyridine) iron

0,1 g (0,50 mmol) of $FeCl_2.4H_2O$ is dissolved in 10 ml of water. This solution is added dropwise to 10 ml of a boiling

solution of ethanol containing 0,29 (1,55 mmol) of 4,4'-diamino-2,2'-bipyridine. A purple-red colour appears. After cooling to room temperature 20 ml of diethylether are added to precipitate the complex. This complex is separated by filtration, washed with a mixture of acetone and diethylether (1:6 vol/vol) and dried under high vacuum.

- Oxidation-reduction potential E° (normal potential)

When the complex is dissolved in an organic solvent such as acetonitrile in the presence of $LiClO_4$ 0.2 M and a potentiodynamic measurement is effected using a vitreous carbon electrode one obtains E° = 225 mV (reference: calomel electrode SCE). In a phosphate buffer PBS (NaCl 100 mM, NaH_2PO_4 10 mM adjusted to pH 7.4), with a vitreous carbon electrode one obtains E° = + 70 mV (reference: calomel electrode SCE).

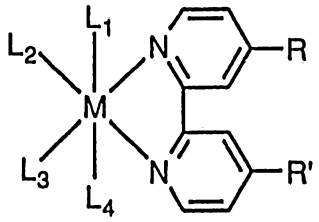
- Absorption spectrum data of UV and visible waves

wavelength λ max (nm)	extinction coefficient $\varepsilon(M^{-1}\ cm^{-1})$
252	110800
366	24800
494	7780
580	10600



THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

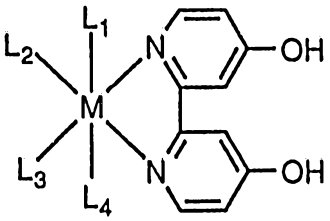
1. A mono, bis or tris (4,4' substituted 2,2'-bipyridine) complex of a metal M having the following formula (I)



(I)

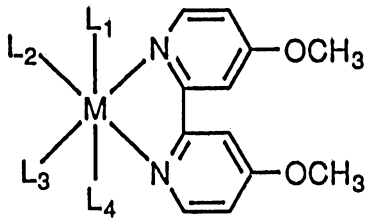
in which M represents osmium, R and R' being the same or different and at least one of which represents an electron donor group, selected from a hydroxy, methoxy, aryloxy group or an amino or dialkylamino group and L_1, L_2, L_3 and L_4 are taken in pairs to form two bidentate ligands, said bidentate ligands forming together with the 4,4'-substituted 2,2'-bipyridine moiety a coordination complex with the metal M.

2. A complex according to Claim 1 wherein R and R' each represents a hydroxy group, the complex then having the formula (II)



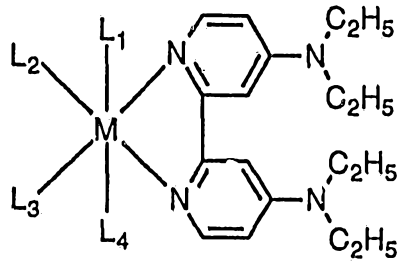
(II)

3. A complex according to Claim 1 wherein R and R' each represents a dimethoxy group, the complex then having the formula (III)



(III)

4. A complex according to Claim 1 wherein R and R' each represents a N,N-ethylamino group, the complex then having the formula (IV)



(IV)

5. A complex according to Claim 1 wherein L_1 and L_2 on the one hand and L_3 and L_4 on the other hand respectively form a bidentate ligand, these two bidentate ligands being the same or different and being ethylenediamine, 1,2-bis(2-pyridyl)ethane, oxalic acid, acetylacetone, glycine or a bipyridine or phenanthroline disubstituted by an R_1 group and an R_2 group, R_1 and R_2 being the same or different and each representing hydrogen, NO_2, Cl, an alkyl group, an aryl group, an OH group, a methoxy group, an aryloxy group or an amino or dialkylamino group.

6. A complex according to Claim 5 which is a tris(4,4'-dihydroxy-2,2'-bipyridine) complex of the metal M, a tris(4,4'-dimethoxy-2,2'-bipyridine) complex of the metal M or a tris(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine) complex of the metal M.

7. A complex according to the Claim 2 wherein L_1 and L_2 together form 4,4'-dihydroxy-2,2'-bipyridine and where L_3 and L_4 together form a bidentate ligand which is ethylenediamine, 1,2-bis(2-pyridyl)ethane, oxalic acid, acetylacetone, glycine or a bipyridine or phenanthroline disubstituted by an R_1 group and an R_2 group, R_1 and R_2 being the same or different and each representing hydrogen, NO_2, Cl, an alkyl group, an aryl group, an OH group, a methoxy group, an aryloxy group or amino or dialkylamino group.

8. A complex according to Claim 7 which is a bis(4,4'-dihydroxy-2,2'-bipyridine)mono(2,2'-bipyridine) complex of the metal M, bis(4,4'-dihydroxy-2,2'-bipyridine)- mono(4,4'-dimethoxy-2,2'-bipyridine) complex of the metal M, bis(4,4'-dihydroxy-2,2'-bipyridine) mono(4,4'-dimethyl-2,2'-bipyridine) complex of the metal M, bis(4,4'-dihydroxy-2,2'-bipyridine) mono(4-alkyl-2,2'-bipyridine) complex of the metal M, the bis(4,4'-dihydroxy-2,2-bipyridine) mono(4,4'-dialkyl-2,2'-bipyridine) complex of the metal M, the bis(4,4'-dihydroxy-2,2'-bipyridine) mono(4,7-dihydroxy-1,10-phenanthroline) complex of the metal M or the bis(4,4'-dihydroxy-1,10-phenanthroline) complex of the metal M or the bis(4,4'-dihydroxy-2,2'-bipyridine) mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine complex of the metal M.

9. A complex according to the Claim 3 where L_1 and L_2 together form 4,4'-dimethoxy-2,2'-bipyridine and L_3 and L_4 together form a bidentate ligand which is ethylenediamine, 1,2-bis(2-pyridyl)ethane, oxalic acid, acetylacetone, glycine or a bipyridine or phenanthroline disubstituted by an R_1 group and an R_2 group, R_1 and R_2 being the same or different and each representing hydrogen, NO_2, Cl, an alkyl group, an aryl group, an OH group, a methoxy group, an aryloxy group or amino or dialkylamino group.

10. A complex according to Claim 9 which is a bis(4,4'-dimethoxy-2,2'-bipyridine)mono(2,2'-bipyridine) complex of the metal M; a bis(4,4'-dimethoxy-2,2'-bipyridine) mono(4,4'-dimethyl-2,2'-bipyridine) complex of the metal M; a bis(4,4'-dimethoxy-2,2'-bipyridine) mono(4-alkyl-2,2'-bipyridine) complex of the metal M; a bis(4,4'-dimethoxy-2,2'-bipyridine)mono(4,4'-dialkyl-2,2'-bipyridine) complex of the metal M; a bis(4,4'-dimethoxy-2,2'-bipyridine)mono(4,7-dihydroxy-1,10-phenanthroline) complex of the metal M; a bis(4,4'-dimethoxy-2,2'-bipyridine)mono(4,4'-dihydroxy-2,2'-bipyridine) complex of the metal M or a bis(4,4'-dimethoxy-2,2'-bipyridine)mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine) complex of the metal M.

11. A complex according to the Claim 4 wherein L_1 and L_2 together form 4,4'-bis(N,N-ethylamino-2,2'-bipyridine) and where L_3 and L_4 together form a bidentate ligand which is ethylenediamine, 1,2-bis(2-pyridyl)ethane, oxalic acid, acetylacetone, glycine or a bipyridine or phenanthroline disubstituted by an R_1 group, R_1 and R_2 being the same or different and each representing hydrogen, NO_2, Cl, an alkyl group, an aryl group, an OH group, a methoxy group, an aryloxy group or an amino or dialkylamino group.

12. A complex according to Claim 11 which is a bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)mono(2,2'-bipyridine) complex of the metal M; a bis(4,4' bis(N,N-ethylamino)-2,2'-bipyridine)mono(4,4'-dimethoxy-2,2'-bipyridine) complex of the metal M; a bis(4,4'-bis(N,N-ethylamino-2,2'-bipyridine)mono(4,4'-dimethyl-2,2'-bipyridine) complex of the metal M; a bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)mono(4-alkyl-2,2'-bipyridine) complex of the metal M; a bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)mono(4,4'-dialkyl-2,2'-bipyridine) complex of the metal M, a bis(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)mono(4,4'-dihydroxy-2,2'-bipyridine) complex of the metal M or a bis(4,4'-bis(N,N-ethylamino)2,2'-bipyridine)mono(4,7-dihydroxy-1,10-phenanthroline) complex of the metal M.

13. A complex according to Claim 2 wherein L_1 and L_2 on the one hand and L_3 and L_4 on the other hand respectively form a bidentate ligand, these two ligands being the same and being ethylenediamine, 1,2 bis(2-pyridyl)ethane, oxalic acid, acetylacetone, glycine or a bipyridine or phenanthroline disubstituted by an R_1 group and an R_2 group, R_1 and R_2 being the same or different and each representing hydrogen, NO_2, Cl, an alkyl group, an aryl group, an OH group, a methoxy group, an aryloxy group or an amino or dialkylamino group.

14. A complex according to Claim 13 which is a mono(4,4'-dihydroxy-2,2'-bipyridine)bis(4,4'-dimethyl-2,2'-bipyridine) complex of the metal M; a mono-(4,4'-dihydroxy-2,2'-bipyridine)bis(2,2'-bipyridine) complex of the metal M, a mono(4,4'-dihydroxy-2,2'-bipyridine)bis(4-alkyl-2,2'-bipyridine) complex of the metal M or a mono(4,4'-dihydroxy-2,2'-bipyridine)bis(4,7-dihydroxy-1,10-phenanthroline) complex of the metal M.

15. A complex according to Claim 3 wherein L_1 and L_2 on the one hand and L_3 and L_4 on the other hand respectively form a bidentate ligand, these two ligands being ethylenediamine, 1,2-bis(2-pyridyl)ethane, oxalic acid, acetylacetone, glycine or a bipyridine or phenanthroline disubstituted by an R_1 group and an R_2 group, R_1 and R_2 being the same or different and each representing hydrogen, NO_2, Cl, an alkyl group, an aryl group, an OH group, a methoxy group, an aryloxy group or an amino or dialkylamino group.

16. A complex according to Claim 15 which is a mono(4,4'- dimethoxy-2,2'-bipyridine) bis(4,4'-dimethyl-2,2'-bipyridine) complex of the metal M; a mono-(4,4'-dimethoxy-2,2'-bipyridine)bis(2,2'-bipyridine) complex of the metal M, a mono(4,4'-dimethoxy-2,2'-bipyridine)bis(4-alkyl- 2,2'- bipyridine) complex of the metal M; a mono(4,4'-dimethoxy-2,2'-bipyridine)bis(4,7-dihydroxy-1,10-phenanthroline) complex of the metal M or a mono(4,4'-dimethoxy-2,2'-bipyridine)mono(4,4'-dihydroxy-2,2'-bipyridine)mono(4,4'-dimethyl-2,2'-bipyridine) complex of the metal M.

17. A complex according to the Claim 4 wherein L_1 and L_2 on the one hand and L_3 and L_4 on the other hand respectively form a bidentate ligand, these two ligands being ethylenediamine, 1,2-bis(2-pyridyl)ethane, oxalic acid, acetylacetone, glycine or a bipyridine or phenanthroline disubstituted by an R_1 group and an R_2 group, R_1 and R_2 being the same or different and each representing hydrogen, NO_2, Cl, an alkyl group, an aryl group, an OH group, a methoxy group, an aryloxy group or an amino or dialkylamino group.

18. A complex according to Claim 17 which is a mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)bis(4,4'-dimethyl-2,2'-bipyridine) complex of the metal M; a mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)bis(2,2'-bipyridine) complex of the metal M; a mono(4,4'-bis(N,N-ethylamino)2,2'-bipyridine) bis(4-alkyl-2,2'-bipyridine) complex of the metal M or a mono(4,4'-bis(N,N-ethylamino)-2,2'-bipyridine)bis(4,6-dihydroxy-1,10-phenanthroline) complex of the metal M.

19. A process for the preparation of a complex according to Claim 1 wherein a soluble salt of the metal M is reacted under heating in an organic solvent successively with useful stoechiometric amounts of ligands L1, L2, L3, L4, or a combination of these ligand as bidentate ligands.

20. A mediator for amperometric sensor wherein it is a complex according to any one of Claims 1 to 18.

DATED this 14th day of December, 1994.

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IAS:MD:JZ/ML (AU1244192.WPC) (Doc.25)



ABSTRACT

Mono, bis and tris(substituted 2,2'-bipyridine) complexes of iron, osmium or vanadium are described wherein the bipyridine is substituted by at least one electron donor group. The donor group is a hydroxy, methoxy, aryloxy group or an amino or dialkylamino group. Processes for the preparation of these complexes.

AUSTRALIAN PATENT OFFICE LS

INTERNATIONAL SEARCH REPORT

International Application No PCT/CH 92/00033

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl.[5] C 07 F 15/00 C 07 F 15/02 C 07 F 9/00 G 01 N 27/30

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
Int.Cl.[5]	C 07 F G 01 N

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category [10]	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X	WO, A, 8602734 (HYPERION CATALYSIS INTERNATIONAL INC.) 9 May 1986, see the whole document	1-26
X	WO, A, 9005732 (THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK) 31 May 1990, see the whole document	1-26
X	EP, A, 0178450 (F. HOFFMANN-LA ROCHE & CO.) 23 April 1986, see the whole document	1-26
X	EP, A, 0074807 (THE SECRETARY OF STATE FOR DEFENCE IN HER BRITANNIC MAJESTY'S GOVERNMENT OF THE UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND) 23 March 1983, see the whole document	1-26
X	GB, A, 956242 (THE AUSTRALIAN NATIONAL UNIVERSITY) 22 April 1984, see the whole document	1-26

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* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"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

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"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

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
6 April 1992 (06.04.92)	23 April 1992 (23.04.92)
International Searching Authority	**Signature of Authorized Officer**
European Patent Office	

III. DOCUMENTS CONSIDERES COMME PERTINENTS [14] (SUITE DES RENSEIGNEMENTS INDIQUES SUR LA DEUXIEME FEUILLE)

Catégorie °	Identification des documents cités, [16] avec indication, si nécessaire des passages pertinents [17]	No. des revendications visées [18]
X	GB,A, 956242 (THE AUSTRALIAN NATIONAL UNIVERSITY) 22 avril 1984, voir le document en entier	1-26
X	Organic Magnetic Resonance, vol. 22, no. 6, juin 1984, M.J. COOK et al.: "Luminescent metal complexes 4+-13C NMR spectra of the tris chelates of substituted 2,2'-bipyridyls and 1,10-phenanthrolines with ruthenium(II) and osmium(II)", pages 388-394, voir le document en entier	1-26
X	Chemical Abstract, vol. 53, (Columbus, Ohio, US), G.F. SMITH et al.: "4,4'-Substituted 2,2'-bipyridines in chelation reactions with ferrous iron", voir abrégé no. 11087d, & ANALYST 83, 661-6(1958), voir le article en entier	1-26
X	Monatshefte für Chemie, vol. 119, no. 1, 1988, W. NUSSBAUMER et al.: "Wasserphotolyse mit Hilfe von funktionellen Tris-(2,2'-bipyridin)ruthenium(II)-Komplexen", pages 1-15, voir le document en entier	1-26
X	Chemical Abstracts, vol. 113, 1990, (Columbus, Ohio, US), L. DELLA CIANA et al.: "Synthesis and characterization of a new family of luminescent cis-(4,4'-X2-5,5'-Y2-2,2'-bipyridine)2Os(CO)CI(PF6) complexes (X = NEt2, OMe, Me, H, CL, Y = H; X = H, Y = Me; X = Y = Me): control of excited-state properties by bipyridyl substituents", voir page 814, abrégé no. 90292a, & INORG. CHEM. 1990, 29(15), 2792-8, voir le article en entier	1-26
X	Chemical Abstracts, vol. 101, 1984, (Columbus, Ohio, US), K.J. TAKEUCHI et al.: "Redox and spectral properties of monooxo polypyridyl complexes of ruthenium and osmium in aqueous media", voir page 574, abrégé no. 16171w, & INORG. CHEM. 1984, 23(13), 1845-51, voir le article en entier	1-26
X	Journal of the Chemical Society Perkin Transactions II, vol. 8, 1984, M.J. COOK et al.: "Luminescent metal complexes. Part 1. Tris-chelates of substituted 2,2'-bipyridyls with ruthenium(II) as dyes for luminescent solar collectors", pages 1293-1301, voir le article en entier	1-26

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III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
X	Journal of the Chemical Society Perkin Transactions II, vol. 8, 1984, M.J. COOK et al.: "Luminescent metal complexes. Part 2. A model for the luminescence properties of the tris-chelates of substituted 2,2'-bipyridyls with ruthenium (II)", pages 1303-1307, see the whole article	1-26
X	Chemical Abstracts, vol. 100, 1984. (Columbus, Ohio, US), E.C. CONSTABLE: "Nucleophilic attack upon coordinated heterocycles definitive evidence for the enhanced electrophilicity of coordinated pyridines", see page 701, abstract No. 150011b. & INORG. CHIM. ACTA 1984, 82(1), 53-7, see the whole article	1-26
	Journal of the Chemical Society Chemical Communications, NO.13, 1988, M.K. NAZEERUDDIN et al.: "Spontaneous oxidation of water to oxygen by the mixed-valence mu-oxo ruthenium dimer L2(H2O)RuIII-O-RuIV(OH)L2 (L = 2,2'-bipyridyl-5,5'-dicarboxylic acid)", pages 872-874, see the whole article	1-26

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. CH 9200033 SA 56313

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 17/04/92
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A- 8602734	09-05-86	AU-A- 5020085	15-05-86
		EP-A- 0199804	05-11-86
		JP-T- 62500663	19-03-87
WO-A- 9005732	31-05-90	AU-A- 4647689	12-06-90
		CA-A- 2002380	07-05-90
EP-A- 0178450	23-04-86	CA-A- 1261744	26-09-89
		US-A- 5075447	24-12-91
		US-A- 4745076	17-05-88
		AU-B- 586831	27-07-89
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EP-A- 0074807	23-03-83	GB-A- 2109396	02-06-83
		JP-A- 58055910	02-04-83
GB-A- 956242		CH-A- 415657	
		CH-A- 447190	
		FR-A- 1482811	
		NL-A- 260509	
		NL-A- 260510	

RAPPORT DE RECHERCHE INTERNATIONALE

Demande internationale no PCT/CH 92/00033

I. CLASSEMENT DE L'INVENTION (si plusieurs symboles de classification sont applicables, les indiquer tous) 7

Selon la classification internationale des brevets (CIB) ou à la fois selon la classification nationale et la CIB

Int.Cl.5 C 07 F 15/00 C 07 F 15/02 C 07 F 9/00
G 01 N 27/30

II. DOMAINES SUR LESQUELS LA RECHERCHE A PORTE

Documentation minimale consultée[8]

Système de classification	Symboles de classification
Int.Cl.5	C 07 F G 01 N

Documentation consultée autre que la documentation minimale dans la mesure où de tels documents font partie des domaines sur lesquels la recherche a porté[9]

III. DOCUMENTS CONSIDERES COMME PERTINENTS[10]

Catégorie °	Identification des documents cités, avec indication, si nécessaire,[12] des passages pertinents[13]	No. des revendications visées[14]
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X	WO,A,9005732 (THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK) 31 mai 1990, voir le document en entier	1-26
X	EP,A,0178450 (F. HOFFMANN-LA ROCHE & CO.) 23 avril 1986, voir le document en entier	1-26
X	EP,A,0074807 (THE SECRETARY OF STATE FOR DEFENCE IN HER BRITANNIC MAJESTY'S GOVERNMENT OF THE UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND) 23 mars 1983, voir le document en entier	1-26

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° Catégories spéciales de documents cités:[11]

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"E" document antérieur, mais publié à la date de dépôt international ou après cette date

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"Y" document particulièrement pertinent; l'invention revendiquée ne peut être considérée comme impliquant une activité inventive lorsque le document est associé à un ou plusieurs autres documents de même nature, cette combinaison étant évidente pour une personne du métier.

"&" document qui fait partie de la même famille de brevets

IV. CERTIFICATION

Date à laquelle la recherche internationale a été effectivement achevée	Date d'expédition du présent rapport de recherche internationale
06-04-1992	23 APR 1992
Administration chargée de la recherche internationale: OFFICE EUROPEEN DES BREVETS	Signature du fonctionnaire autorisé: Miss T. TAZELAAR

Formulaire PCT/ISA/210 (deuxième feuille) (Janvier 1985)

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
X	Organic Magnetic Resonance , vol. 22, No. 6, June 1984, M.J. COOK et al.:"Luminescent metal complexes 4+-13C NMR spectra of the tris chelates of substituted 2,2'-bipyridyls and 1,10-phenanthrolines with ruthenium(II) and osmium(II)", pages 388-394, see the whole document	1-26
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A	Journal of the Chemical Society, Chemical Communications, no. 13, 1988, M.K. NAZEERUDDIN et al.: "Spontaneous oxidation of water to oxygen by the mixed-valence mu-oxo ruthenium dimer L2(H2O)RuIII-O-RuIV(OH)L2 (L = 2,2'-bipyridyl-5,5'-dicarboxylic acid)", pages 872-874, voir le article en entier	1-26

ANNEXE AU RAPPORT DE RECHERCHE INTERNATIONALE RELATIF A LA DEMANDE INTERNATIONALE NO.

CH 9200033
SA 56313

La présente annexe indique les membres de la famille de brevets relatifs aux documents brevets cités dans le rapport de recherche internationale visé ci-dessus.
Lesdits membres sont contenus au fichier informatique de l'Office européen des brevets à la date du 17/04/92
Les renseignements fournis sont donnés à titre indicatif et n'engagent pas la responsabilité de l'Office européen des brevets.

Document brevet cité au rapport de recherche	Date de publication	Membre(s) de la famille de brevet(s)		Date de publication
WO-A- 8602734	09-05-86	AU-A-	5020085	15-05-86
		EP-A-	0199804	05-11-86
		JP-T-	62500663	19-03-87
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		AU-B-	586831	27-07-89
		AU-A-	4733485	27-03-86
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GB-A- 956242		CH-A-	415657	
		CH-A-	447190	
		FR-A-	1482811	
		NL-A-	260509	
		NL-A-	260510	

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