

2,2'-Diamino biaryls with two secondary amines and production thereof by electrochemical coupling

The invention relates to novel 2,2'-diaminobiaryls, and to an electrochemical process for
5 preparing 2,2'-diaminobiaryls.

The direct electrochemical C,C cross-coupling of differently protected anilines is unknown to date. Although a copper-catalysed C,C coupling is possible in order to prepare unsymmetric 2,2'-diaminobiaryls, these are either unprotected (M. Smrcina, S. Vyskocil, B. Maca,
10 M. Polasek, T. A. Claxton, A. P. Abbott, P. Kocovsky, J. Org. Chem. 1994, 59, 2156–2163.) or both amino groups bear the same protecting group (J.-F. Cui, H. Huang, H. Wong, Synlett 2011, 7, 1018–1022. and W. Kalk, H.-S. Bien, K.-H. Schündehütte, Justus Liebigs Ann. Chem. 1977, 329–337.).

There is likewise knowledge only of the synthesis of symmetrically protected 2,2'-
15 diaminobiaryls having the same protecting group by an Ullmann-like reaction regime (W. Kalk, H.-S. Bien, K.-H. Schündehütte, Justus Liebigs Ann. Chem. 1977, 329–337, and S. Zhang, D. Zhang, L. S. Liebeskind, J. Org. Chem. 1997, 62, 2312–2313.). The selection of protecting groups and substitution patterns of the substances to be coupled that are used is greatly restricted for this reason.

20 The synthesis of unsymmetric 2,2'-diaminobiaryls is also possible via a [3,3] sigmatropic rearrangement, but this has poor selectivities. By this route, there is only access to singly protected 2,2'-diaminobiaryls with a greatly restricted choice of protecting groups.

See:

- Y.-K. Lim, J.-W. Jung, H. Lee, C.-G. Cho, J. Org. Chem. 2004, 69, 5778–5781;
- 25 - S.-E. Suh, I.-K. Park, B.-Y. Lim, C.-G. Cho, Eur. J. Org. Chem. 2011, 3, 455–457;
- B.-Y. Lim, M.-K. Choi, C.-G. Cho, Tetrahedron Letters 2011, 52, 6015–6017.

For preparation of differently double-protected 2,2'-diaminonaphthyls, unprotected 2,2'-diaminobiaryls were first singly protected, and a second protecting group was then
30 introduced in the second synthesis step (M. Shi, W.-L. Duan, G.-B. Rong, Chirality 2004, 16, 642–651). In this case, the protection is thus effected only after the coupling. The result of this is that only particular combinations of protecting groups are tolerated, since the second group can be introduced only under such conditions under which the first group is stable. As a result, only a few combinations are tolerated. Moreover, this procedure is notable for lack

of selectivity, purification processes between the synthesis steps and small yields, which makes this known method uncompetitive. Moreover, a multitude of synthesis steps of protecting, deprotecting and reprotecting are necessary in some cases, in order to arrive at the desired target compound.

5

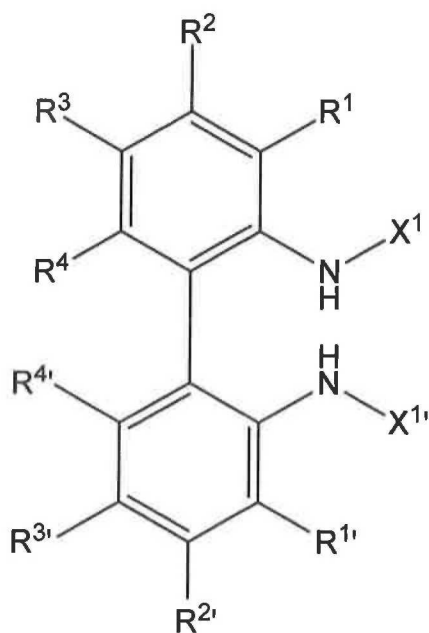
The problem addressed by the invention was that of providing 2,2'-diaminobiaryls having novel structures compared to the 2,2'-diaminobiaryls known in the literature. In addition, a process by which the novel 2,2'-diaminobiaryls can be prepared in good yield was to be developed. More particularly, the process was to stand out advantageously from the preparation processes known from the prior art.

10

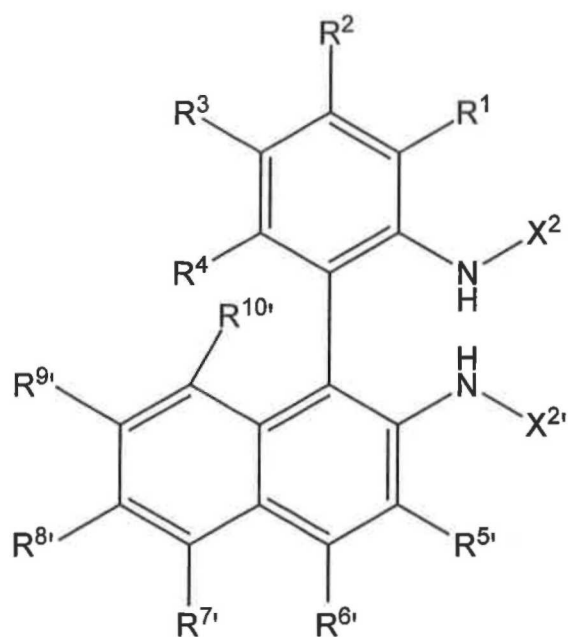
The object is achieved by a compound according to Claim 1.

Compound having one of the general structures (I) to (III):

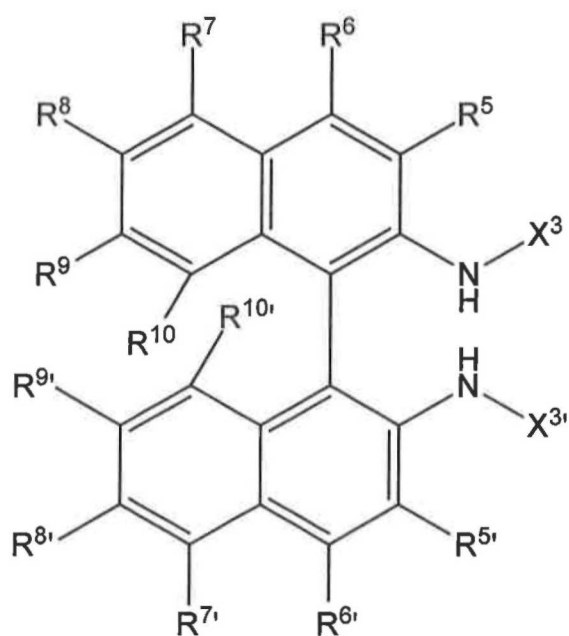
15



(I)



(II)



(III)

10 where

$R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}$ are selected from:

-H, $-(C_1-C_{12})$ -alkyl, $-O-(C_1-C_{12})$ -alkyl, $-O-(C_6-C_{20})$ -aryl, $-(C_6-C_{20})$ -aryl, -S-alkyl, -S-aryl, halogen, $-COO-(C_1-C_{12})$ -alkyl, $-CONH-(C_1-C_{12})$ -alkyl, $-CO-(C_1-C_{12})$ -alkyl, $-CO-(C_6-C_{20})$ -aryl, $-COOH$, $-OH$, $-SO_3H$, $-CN$, $-N[(C_1-C_{12})$ -alkyl] $_2$;

$R^5, R^6, R^7, R^8, R^9, R^{10}, R^{5'}, R^{6'}, R^{7'}, R^{8'}, R^{9'}, R^{10'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen, -COO-(C₁-C₁₂)-alkyl, -CONH-(C₁-C₁₂)-alkyl, -CO-(C₁-C₁₂)-alkyl, -CO-(C₆-C₂₀)-aryl, -COOH, -OH, -SO₃H, -N[(C₁-C₁₂)-alkyl]₂;

5 where the alkyl and aryl groups mentioned may be substituted;

X^1 and $X^{1'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl, and X^1 is not the same radical as $X^{1'}$;

10 and the following two radical pairs are excluded:

X^1 = acetyl and $X^{1'}$ = benzoyl,

X^1 = benzoyl and $X^{1'}$ = acetyl;

X^2 and $X^{2'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, 15 trifluoroacetyl, benzoyl, sulphonyl, sulphenyl, and X^2 is not the same radical as $X^{2'}$;

X^3 and $X^{3'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl,

20 and X^3 is not the same radical as $X^{3'}$.

-(C₁-C₁₂)-Alkyl and -O-(C₁-C₁₂)-alkyl may each be unsubstituted or substituted by one or more identical or different radicals selected from -(C₃-C₁₂)-cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -(C₆-C₂₀)-aryl, fluorine, chlorine, cyano, formyl, acyl and alkoxycarbonyl.

25

-(C₆-C₂₀)-Aryl and -(C₆-C₂₀)-aryl-(C₆-C₂₀)-aryl- may each be unsubstituted or substituted by one or more identical or different radicals selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl, -halogen (such as Cl, F, Br, I), -COO-(C₁-C₁₂)-alkyl, -CONH-(C₁-C₁₂)-alkyl, -(C₆-C₂₀)-aryl-CON[(C₁-C₁₂)-alkyl]₂, -CO-(C₁-C₁₂)-alkyl, -CO-(C₆-C₂₀)-aryl, -COOH, -OH, -SO₃H, -SO₃Na, -NO₂, -CN, -N[(C₁-C₁₂)-alkyl]₂.

30

In the context of the invention, the expression "-(C₁-C₁₂)-alkyl" encompasses straight-chain and branched alkyl groups. Preferably, these groups are unsubstituted straight-chain or branched -(C₁-C₈)-alkyl groups and most preferably -(C₁-C₆)-alkyl groups. Examples of -(C₁-C₁₂)-alkyl

groups are especially methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, 2-pentyl, 2-methylbutyl, 3-methylbutyl, 1,2-dimethylpropyl, 1,1-dimethylpropyl, 2,2-dimethylpropyl, 1-ethylpropyl, n-hexyl, 2-hexyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 2,2-dimethylbutyl, 1,3-dimethylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-trimethylpropyl, 1-ethylbutyl, 1-ethyl-2-methylpropyl, n-heptyl, 2-heptyl, 3-heptyl, 2-ethylpentyl, 1-propylbutyl, n-octyl, 2-ethylhexyl, 2-propylheptyl, nonyl, decyl.

The elucidations relating to the expression $-(C_1-C_{12})$ -alkyl also apply to the alkyl groups in $-O-(C_1-C_{12})$ -alkyl, i.e. in $-(C_1-C_{12})$ -alkoxy. Preferably, these groups are unsubstituted straight-chain or branched $-(C_1-C_6)$ -alkoxy groups.

Substituted $-(C_1-C_{12})$ -alkyl groups and substituted $-(C_1-C_{12})$ -alkoxy groups may have one or more substituents, depending on their chain length. The substituents are preferably each independently selected from $-(C_3-C_{12})$ -cycloalkyl, $-(C_3-C_{12})$ -heterocycloalkyl, $-(C_6-C_{20})$ -aryl, fluorine, chlorine, cyano, formyl, acyl and alkoxycarbonyl.

The expression " $-(C_3-C_{12})$ -cycloalkyl", in the context of the present invention, encompasses mono-, bi- or tricyclic hydrocarbyl radicals having 3 to 12, especially 5 to 12, carbon atoms. These include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclododecyl, cyclopentadecyl, norbornyl and adamantyl. One example of a substituted cycloalkyl would be menthyl.

The expression " $-(C_3-C_{12})$ -heterocycloalkyl groups", in the context of the present invention, encompasses nonaromatic saturated or partly unsaturated cycloaliphatic groups having 3 to 12, especially 5 to 12, carbon atoms. The $-(C_3-C_{12})$ -heterocycloalkyl groups have preferably 3 to 8, more preferably 5 or 6, ring atoms. In the heterocycloalkyl groups, as opposed to the cycloalkyl groups, 1, 2, 3 or 4 of the ring carbon atoms are replaced by heteroatoms or heteroatom-containing groups. The heteroatoms or the heteroatom-containing groups are preferably selected from $-O-$, $-S-$, $-N-$, $-N(=O)-$, $-C(=O)-$ and $-S(=O)-$. Examples of $-(C_3-C_{12})$ -heterocycloalkyl groups are tetrahydrothiophenyl, tetrahydrofuryl, tetrahydropyranyl and dioxanyl.

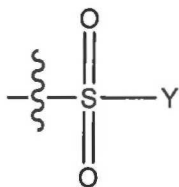
In the context of the present invention, the expression " $-(C_6-C_{20})$ -aryl and $-(C_6-C_{20})$ -aryl- (C_6-C_{20}) -aryl-" encompasses mono- or polycyclic aromatic hydrocarbyl radicals. These have 6 to 20 ring atoms, more preferably 6 to 14 ring atoms, especially 6 to 10 ring atoms. Aryl is preferably $-(C_6-C_{10})$ -aryl and $-(C_6-C_{10})$ -aryl- (C_6-C_{10}) -aryl-. Aryl is especially phenyl, naphthyl, indenyl, fluorenyl, anthracenyl, phenanthrenyl, naphthacenyl, chrysenyl, pyrenyl, coronenyl. More particularly, aryl is phenyl, naphthyl and anthracenyl.

Substituted $-(C_6-C_{20})$ -aryl groups and $-(C_6-C_{20})$ -aryl- (C_6-C_{20}) -aryl groups may have one or more (e.g. 1, 2, 3, 4 or 5) substituents, depending on the ring size. These substituents are preferably each independently selected from -H, $-(C_1-C_{12})$ -alkyl, $-O-(C_1-C_{12})$ -alkyl, $-O-(C_6-C_{20})$ -aryl, $-(C_6-C_{20})$ -aryl, -halogen (such as Cl, F, Br, I), $-COO-(C_1-C_{12})$ -alkyl, $-CONH-(C_1-C_{12})$ -alkyl, $-(C_6-C_{20})$ -aryl- $CON[(C_1-C_{12})$ -alkyl]₂, $-CO-(C_1-C_{12})$ -alkyl, $-CO-(C_6-C_{20})$ -aryl, $-COOH$, $-OH$, $-SO_3H$, $-SO_3Na$, $-NO_2$, $-CN$, $-N[(C_1-C_{12})$ -alkyl]₂.

Substituted $-(C_6-C_{20})$ -aryl groups and $-(C_6-C_{20})$ -aryl- (C_6-C_{20}) -aryl groups are preferably substituted $-(C_6-C_{10})$ -aryl groups and $-(C_6-C_{10})$ -aryl- (C_6-C_{10}) -aryl groups, especially substituted phenyl or substituted naphthyl or substituted anthracenyl. Substituted $-(C_6-C_{20})$ -aryl groups preferably bear one or more, for example 1, 2, 3, 4 or 5, substituents selected from $-(C_1-C_{12})$ -alkyl groups, $-(C_1-C_{12})$ -alkoxy groups.

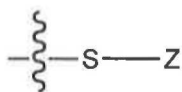
The expression "halogens" encompasses Cl, F, Br, I, preferably Cl, Br, I.

Sulphonyl groups are understood to mean the following groups:



with $Y = OH$, halogens, alkyl, aryl, cycloalkyl, where the radicals include the abovementioned definitions and may also be substituted.

Sulphenyl groups are understood to mean the following groups:



with $Z = \text{OH}$, halogens, alkyl, aryl, cycloalkyl with $Z \neq \text{H}$, where the radicals include the abovementioned definitions and may also be substituted.

5 In one embodiment, X^1 and $X^{1'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, X^1 is selected from:

10 *tert*-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, $X^{1'}$ is selected from:

15 *tert*-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, X^2 and $X^{2'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

20

In one embodiment, X^2 is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

25 In one embodiment, $X^{2'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, X^3 and $X^{3'}$ are selected from:

30 *tert*-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, X^3 is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, $X^{3'}$ is selected from:

- 5 *tert*-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, X^1 and $X^{1'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

10

In one embodiment, X^1 is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, $X^{1'}$ is selected from:

- 15 *tert*-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, X^2 and $X^{2'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

- 20 In one embodiment, X^2 is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, $X^{2'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

25

In one embodiment, X^3 and $X^{3'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, X^3 is selected from:

- 30 *tert*-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, $X^{3'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one embodiment, X^1 and $X^{1'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one embodiment, X^1 is selected from:

- 5 *tert*-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one embodiment, $X^{1'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

- 10 In one embodiment, X^2 and $X^{2'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one embodiment, X^2 is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

15

In one embodiment, $X^{2'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one embodiment, X^3 and $X^{3'}$ are selected from:

- 20 *tert*-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one embodiment, X^3 is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

- 25 In one embodiment, $X^{3'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In a preferred embodiment, the X^1 and $X^{1'}$, X^2 and $X^{2'}$, X^3 and $X^{3'}$ radicals are protecting groups. In other words, those chemical groups which can be detached again. By virtue of X^1 and $X^{1'}$, X^2 and $X^{2'}$, X^3 and $X^{3'}$ each being different radicals in pairs, the different protecting groups can be detached selectively (orthogonal protecting groups).

30

Orthogonality of protecting groups means that, when a plurality of protecting groups of different types are used, each protecting group can be detached individually and in any

sequence on the basis of the different detachment reagents, without attack on any of the other protecting groups.

For example, X^1 can be detached and $X^{1'}$ remains in the molecule or can be detached in a further reaction step. It is likewise conceivable, conversely, that $X^{1'}$ is detached selectively and X^1 remains in the molecule.

The same applies analogously to the pairs of X^2 and $X^{2'}$, X^3 and $X^{3'}$.

In one embodiment, $R^1, R^2, R^3, R^4, R^{1'}, R^{2'}, R^{3'}, R^{4'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen.

In one embodiment, $R^1, R^2, R^3, R^4, R^{1'}, R^{2'}, R^{3'}, R^{4'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl.

In one embodiment, $R^{5'}, R^{6'}, R^{7'}, R^{8'}, R^{9'}, R^{10'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen.

In one embodiment, $R^{5'}, R^{6'}, R^{7'}, R^{8'}, R^{9'}, R^{10'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl.

In one embodiment, are $R^5, R^6, R^7, R^8, R^9, R^{10}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen.

In one embodiment, are $R^5, R^6, R^7, R^8, R^9, R^{10}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl.

In one embodiment, the compound has one of the two general structures (I) and (II).

In one embodiment, the compound has the general structure (I).

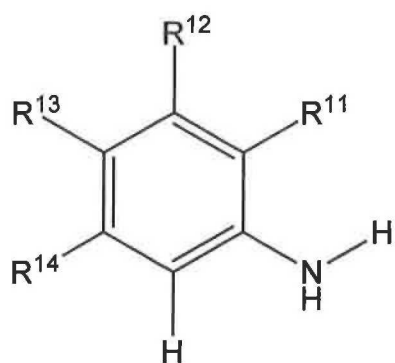
In one embodiment, the compound has the general structure (II).

In one embodiment, the compound has the general structure (III).

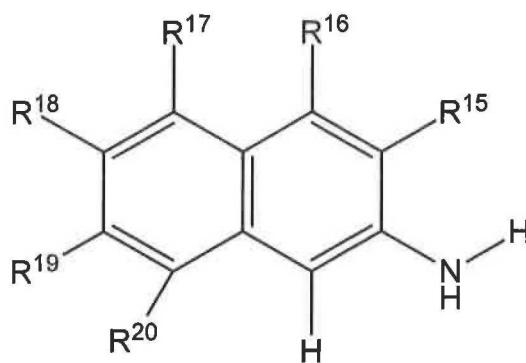
As well as the compounds, a process for their preparation of 2,2'-diaminobiaryls is also claimed.

Process for preparing 2,2'-diaminobiaryls, comprising the process steps of:

- 5 a) reacting a compound of the formula (IVa) or (Va):



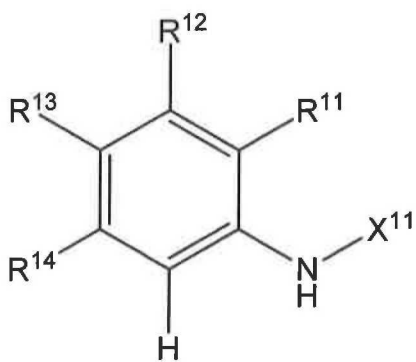
(IVa)



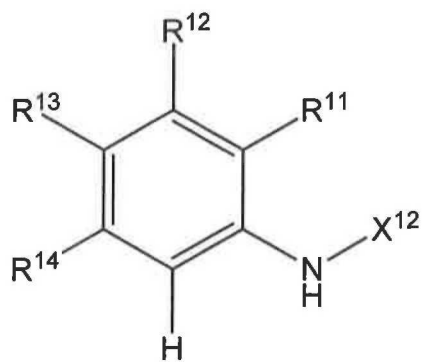
(Va)

10

with reaction of (IVa) with X^{11} or X^{12} to give (IVb1) or (IVb2), or reaction of (Va) with X^{13} to give (Vb):

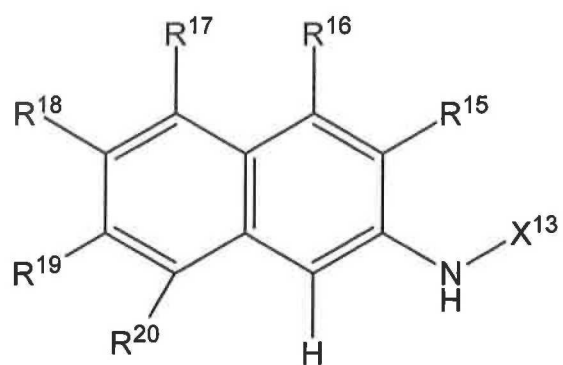


(IVb1)



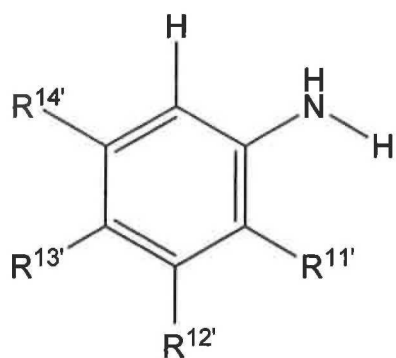
(IVb2)

15

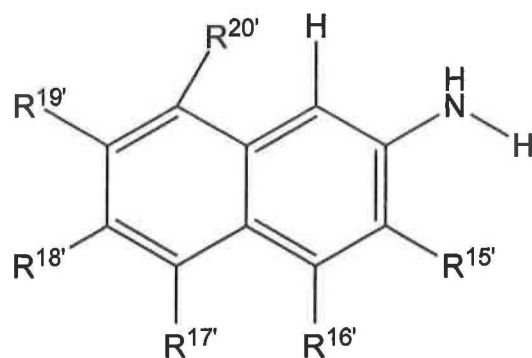


(Vb)

5 b) reacting a compound of the formula (VIa) or (VIIa):



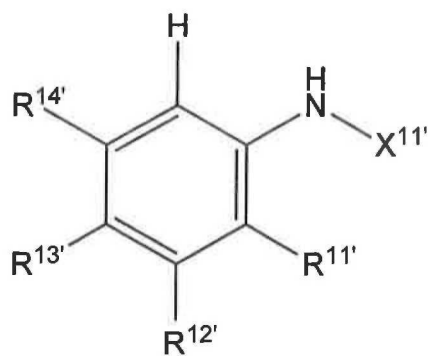
(VIa)



(VIIa)

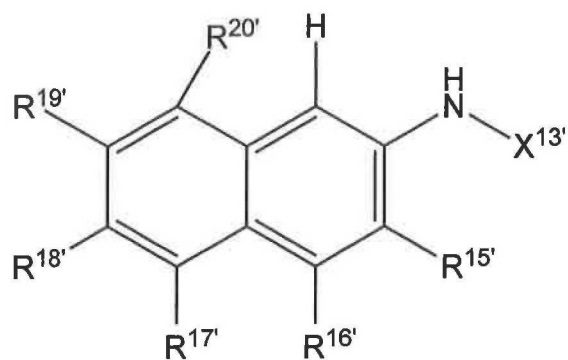
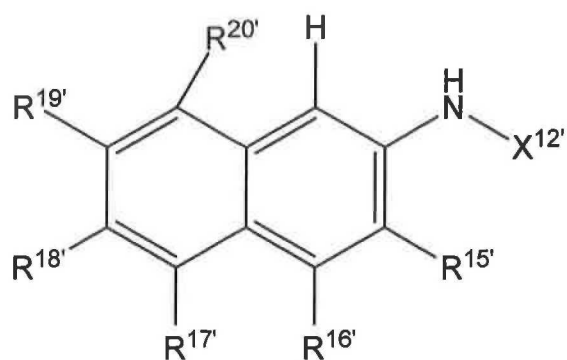
10

with reaction of (VIa) with X^{11'} to give (VIb), or
of (VIIa) with X^{12'} or X^{13'} to give (VIIb1) or (VIIb2):



15

(VIb)



5

(VIIb1)

(VIIb2)

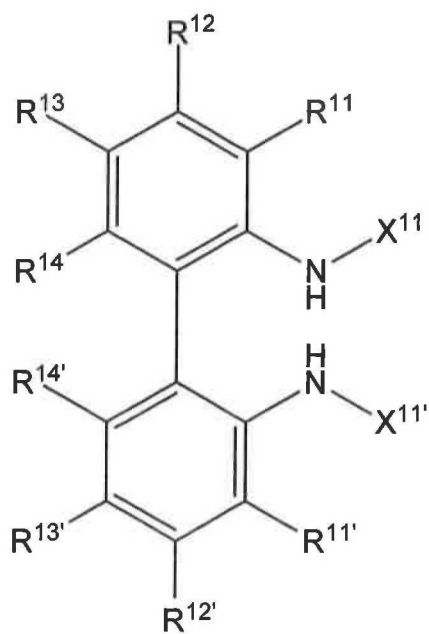
c) electrochemical coupling of:

- (IVb1) with (VIb) to give (I*), or

- (IVb2) with (VIIb1) to give (II*), or

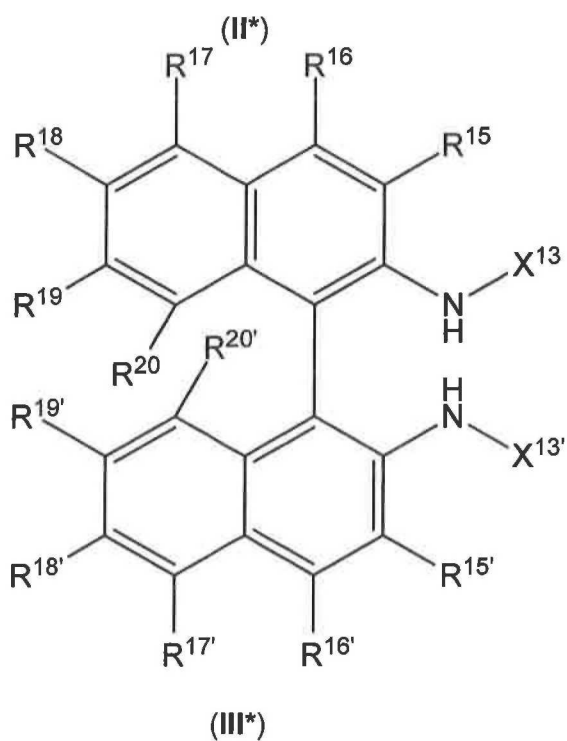
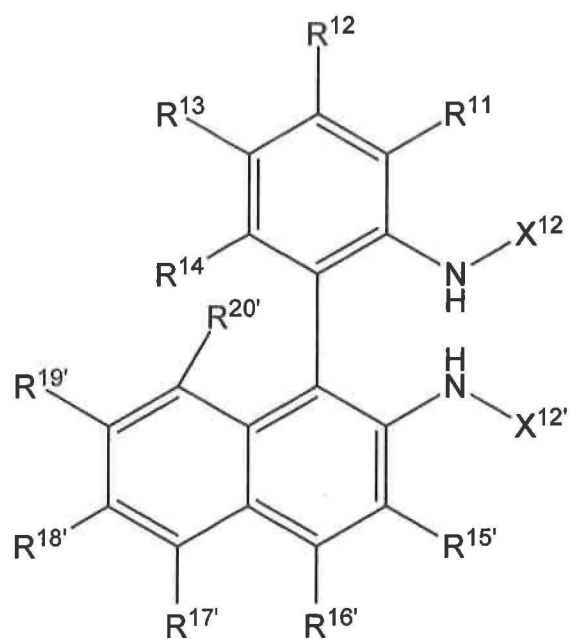
10 - (Vb) with (VIIb2) to give (III*),

in each case with use of the compound having the higher oxidation potential in excess:



(I*)

15



5

where

- 10 R^{11} , R^{12} , R^{13} , R^{14} , $R^{11'}$, $R^{12'}$, $R^{13'}$, $R^{14'}$ are selected from:
 -H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen,
 -COO-(C₁-C₁₂)-alkyl, -CONH-(C₁-C₁₂)-alkyl, -CO-(C₁-C₁₂)-alkyl, -CO-(C₆-C₂₀)-aryl, -COOH, -OH,
 -SO₃H, -CN, -N[(C₁-C₁₂)-alkyl]₂;

R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} , $R^{15'}$, $R^{16'}$, $R^{17'}$, $R^{18'}$, $R^{19'}$, $R^{20'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen, -COO-(C₁-C₁₂)-alkyl, -CONH-(C₁-C₁₂)-alkyl, -CO-(C₁-C₁₂)-alkyl, -CO-(C₆-C₂₀)-aryl, -COOH, -OH, -SO₃H, -N[(C₁-C₁₂)-alkyl]₂;

5 where the alkyl and aryl groups mentioned may be substituted;

X^{11} and $X^{11'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl, and X^{11} is not the same radical as $X^{11'}$;

10 X^{12} and $X^{12'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl, and X^{12} is not the same radical as $X^{12'}$;

X^{13} and $X^{13'}$ are selected from:

15 *tert*-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl, and X^{13} is not the same radical as $X^{13'}$.

The process according to the invention does not have the disadvantages discussed in connection with M. Shi, W.-L. Duan, G.-B. Rong, Chirality 2004, 16, 642–651, since the aminoaryls are first selectively protected and only then electrochemically coupled. As a result, entirely novel protecting group combinations are possible in the 2,2'-diaminobiaryls, which cannot be prepared by the route described in the prior art. Furthermore, the workup is greatly simplified, since the introduction of the protecting group is possible much more selectively. In the case of protection of a 2,2'-diaminobiaryl as described in the prior art, there exist two reactive groups in the molecule, i.e. two amino functions, which could also both react at least in traces under particular conditions. This makes the subsequent workup much more difficult and, under some circumstances, several purification steps are needed, which lowers the yields and produces much more waste (solvents). In addition, unlike in the prior art, 2,2'-diaminobiaryls having groups containing a C=O or S group are claimed here, the groups on the two nitrogen atoms being different.

In one variant of the process, X^{11} and $X^{11'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, X¹¹ is selected from:

- 5 *tert*-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, X^{11'} is selected from:

- 10 *tert*-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, X¹² and X^{12'} are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

15

In one variant of the process, X¹² is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

- 20 In one variant of the process, X^{12'} is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, X¹² and X^{13'} are selected from:

- 25 *tert*-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, X¹³ is selected from:

- 30 *tert*-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, X^{13'} is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, X^{11} and $X^{11'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

- 5 In one variant of the process, X^{11} is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, $X^{11'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

10

In one variant of the process, X^{12} and $X^{12'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, X^{12} is selected from:

- 15 *tert*-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, $X^{12'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

- 20 In one variant of the process, X^{12} and $X^{13'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, X^{13} is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

25

In one variant of the process, $X^{13'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

In one variant of the process, X^{11} and $X^{11'}$ are selected from:

- 30 *tert*-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one variant of the process, X^{11} is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one variant of the process, $X^{11'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one variant of the process, X^{12} and $X^{12'}$ are selected from:

5 *tert*-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one variant of the process, X^{12} is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

10 In one variant of the process, $X^{12'}$ is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one variant of the process, X^{12} and $X^{13'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

15

In one variant of the process, X^{13} is selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In one variant of the process, $X^{13'}$ is selected from:

20 *tert*-butyloxycarbonyl, methyloxycarbonyl, phenyloxycarbonyl, trifluoroacetyl, benzoyl.

In a preferred variant of the process, the X^{11} and $X^{11'}$, X^{12} and $X^{12'}$, X^{13} and $X^{13'}$ radicals are protecting groups. In other words, those chemical groups which can be detached again under the respective suitable conditions. By virtue of X^{11} and $X^{11'}$, X^{12} and $X^{12'}$, X^{13} and $X^{13'}$ each being different radicals in pairs, the different protecting groups can be detached selectively (orthogonal protecting groups).

25

Orthogonality of protecting groups means that, when a plurality of protecting groups of different types are used, each protecting group can be detached individually and in any sequence on the basis of the different detachment reagents, without attack on any of the other protecting groups.

30

For example, X^{11} can be detached and $X^{11'}$ remains in the molecule or can be detached in a further reaction step. It is likewise conceivable, conversely, that $X^{11'}$ is detached selectively and X^{11} remains in the molecule.

The same applies analogously to the pairs of X^{12} and $X^{12'}$, X^{13} and $X^{13'}$.

In one variant of the process, R^{11} , R^{12} , R^{13} , R^{14} , $R^{11'}$, $R^{12'}$, $R^{13'}$, $R^{14'}$ are selected from:
-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen.

- 5 In variant of the process, R^{11} , R^{12} , R^{13} , R^{14} , $R^{11'}$, $R^{12'}$, $R^{13'}$, $R^{14'}$ are selected from:
-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl.

In one variant of the process, $R^{15'}$, $R^{16'}$, $R^{17'}$, $R^{18'}$, $R^{19'}$, $R^{20'}$ are selected from:
-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen.

10

In one variant of the process, $R^{15'}$, $R^{16'}$, $R^{17'}$, $R^{18'}$, $R^{19'}$, $R^{20'}$ are selected from:
-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl.

In one variant of the process, R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} are selected from:

- 15 -H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen.

In one variant of the process, R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} are selected from:
-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl.

- 20 In one variant of the process, this process comprises the additional process step of
d1) selective detachment of X^{11} .

In one variant of the process, this process comprises the additional process step of
d2) selective detachment of $X^{11'}$.

25

In one variant of the process, this process comprises the additional process step of
d3) selective detachment of X^{12} .

In one variant of the process, this process comprises the additional process step of

- 30 d4) selective detachment of $X^{12'}$.

In one variant of the process, this process comprises the additional process step of
d5) selective detachment of X^{13} .

In one variant of the process, this process comprises the additional process step of
d6) selective detachment of $X^{13'}$.

By electrochemical coupling (process step c)), biaryldiamines are prepared without adding the
5 organic oxidizing agent, having to work with exclusion of moisture or maintain anaerobic
reaction conditions. This direct method of C,C coupling opens up an inexpensive and
environmentally beneficial alternative to existing multistage conventionally organic synthesis
routes.

10 Process step c) can be conducted using different carbon electrodes (glassy carbon, boron-
doped diamond, graphites, carbon fibres, nanotubes, inter alia), metal oxide electrodes and
metal electrodes. This involves applying current densities in the range of 1-50 mA/cm².

The electrochemical coupling (process step c)) is conducted in the customary, known
15 electrolysis cells.

In one variant of the process, the second aminoaryl is used in at least twice the amount
compared to the first aminoaryl.

20 In one variant of the process, the ratio of the first aminoaryl to the second aminoaryl is in the
range from 1:2 to 1:4.

If required, a conductive salt can be added to the reaction.

25 In one variant of the process, the conductive salt is selected from the group of the alkali metal,
alkaline earth metal, tetra(C₁-C₆-alkyl)ammonium, 1,3-di(C₁-C₆-alkyl)imidazolium and tetra(C₁-
C₆-alkyl)phosphonium salts.

In one variant of the process, the counterions of the conductive salts are selected from the
30 group of sulphate, hydrogensulphate, alkylsulphates, arylsulphates, alkylsulphonates,
arylsulphonates, halides, phosphates, carbonates, alkylphosphates, alkylcarbonates, nitrate,
tetrafluoroborate, hexafluorophosphate, hexafluorosilicate, fluoride and perchlorate.

In one variant of the process, the conductive salt is selected from tetra-(C₁-C₆-alkyl)ammonium salts, and the counterion is selected from sulphate, alkylsulphate, arylsulphate.

The workup and recovery of the biaryldiamines is very simple and is effected, after the reaction has ended, by generally standard separation methods. First of all, the electrolyte solution is distilled and the individual compounds are obtained separately in the form of different fractions. A further purification can be effected, for example, by crystallization, distillation, sublimation or chromatography.

A problem that occurs in the electrochemical coupling of different molecules is that the co-reactants generally have different oxidation potentials E_{Ox} . The result of this is that the molecule having the lower oxidation potential has a higher propensity to release an electron (e^-) to the anode and an H^+ ion to the solvent, for example, than the molecule having the lower oxidation potential. The oxidation potential E_{Ox} can be calculated via the Nernst equation:

$$E_{Ox} = E^\circ + (0.059/n) * \lg([Ox]/[Red])$$

E_{Ox} : Electrode potential for the oxidation reaction (= oxidation potential)

E° : Standard electrode potential

n : Number of electrons transferred

$[Ox]$: Concentration of the oxidized form

$[Red]$: Concentration of the reduced form

If a process known from the coupling of two identical anilines were to be applied to two different anilines, this would result in predominant formation of radicals of the molecule having a lower oxidation potential, and these would then react with themselves. By far the predominant main product obtained would thus be a biaryldiamine which has formed from two identical anilines.

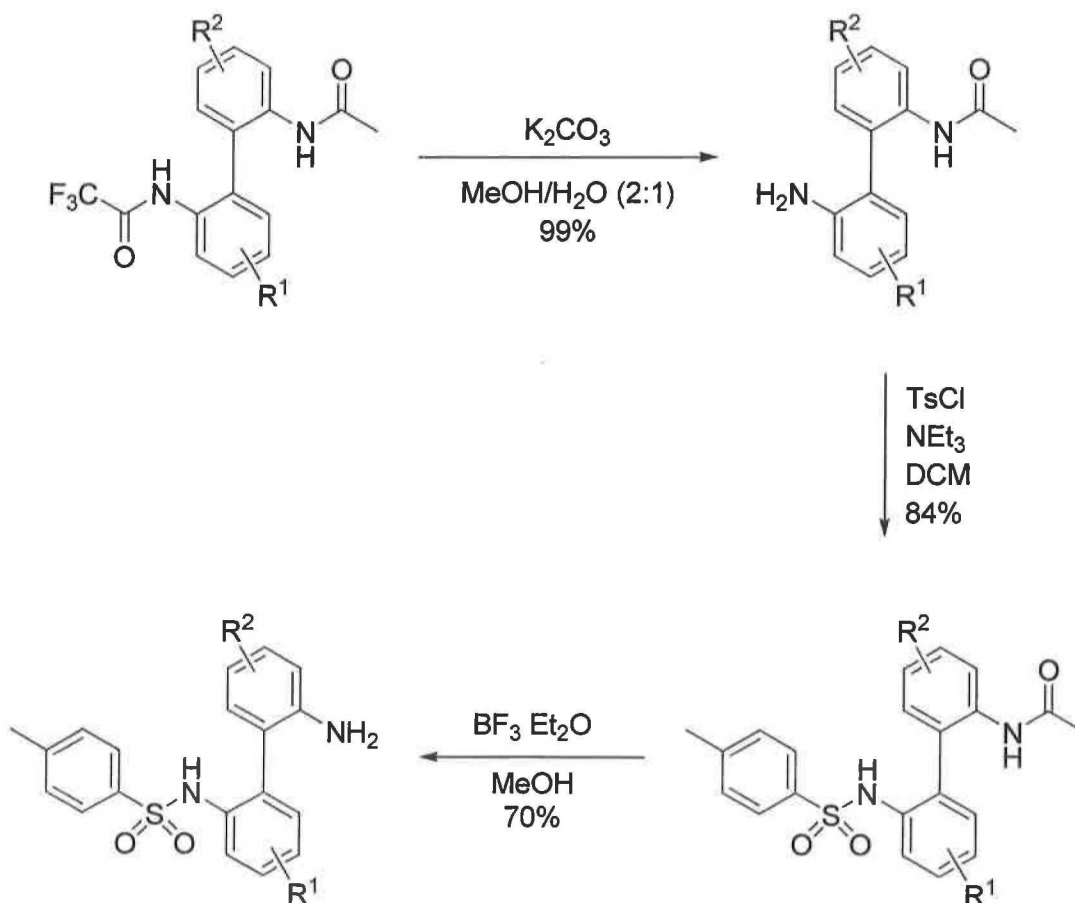
The oxidation potentials of the respective aniline and/or naphthylamine derivatives depend both on the protecting group used in each case and on the structure of the substrate itself. According to the protecting group used, a change in the oxidation potential by several hundred millivolts is possible. This adjustment of the oxidation potentials is possible via electron-withdrawing or electron-donating groups, but also via different sizes and the associated steric effects. The process according to the invention thus opens up an additional

means of controlling the oxidation potential of the aniline and naphthylamine derivatives via the protecting groups.

In addition, it is possible to shift the oxidation potentials of the substrates used through the controlled addition of protic additives such as methanol or water to the electrolyte (such as HFIP: 1,1,1,3,3,3-hexafluoro-2-propanol).

In addition, selective deprotection is possible through the presence of different protecting groups (orthogonal protecting groups). Selective deprotection can be achieved through the choice of bases, Lewis or Brønsted acids, and solvents used. If access to a particular amino functional is not possible by a direct route, it is possible to choose an indirect route, for example via para-toluenesulphonamides, as shown in Reaction Scheme 1.

Reaction Scheme 1:

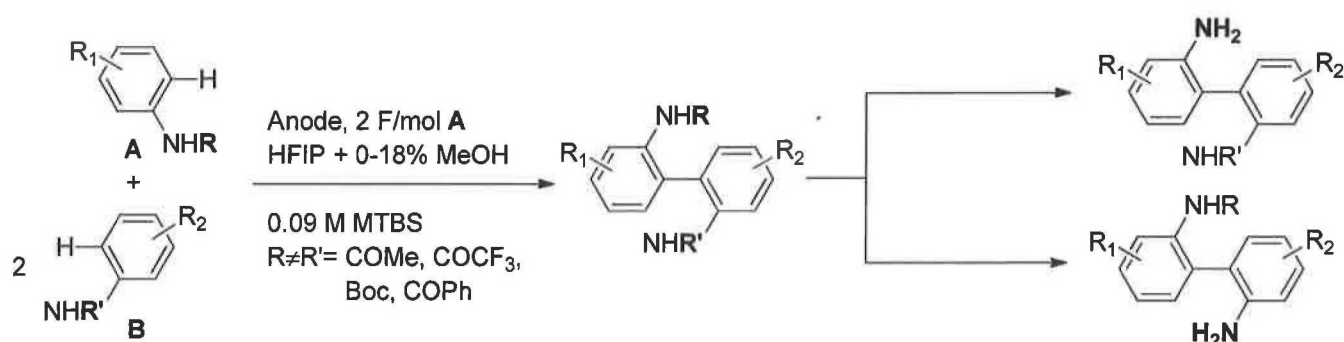


Through electrochemical treatment of differently protected aniline or naphthylamine derivatives, it is possible to selectively prepare unsymmetric 2,2'-diaminobiaryls provided with different protecting groups. The specific choice of the protecting groups enables the control of the oxidation potentials. The invention also enables controlled access to the individual amino functions of the

5 2,2'-diaminobiaryls by a subsequent selective deprotection.

Reaction Scheme 2 shows a general scheme for the C,C cross-coupling reaction. In this case, component **A** is the deficiency component having lower oxidation potential than the excess component **B** which is used in twice the ratio. R and R' are the respective protecting groups which

10 have been chosen specifically.



Reaction Scheme 2: Controlled electrochemical synthesis of differently protected unsymmetric 2,2'-diaminobiaryls, followed by selective deprotection of individual amino functions.

15 MTBS: Bu₃NCH₃ O₃SOCH₃
 HFIP: 1,1,1,3,3,3-hexafluoro-2-propanol

The invention is illustrated in detail hereinafter by working examples and figures.

20 Figure 1 shows the schematic setup of a reaction apparatus in which the coupling reaction to give the corresponding unsymmetric 2,2'-diaminobiaryls can be conducted. The reaction apparatus comprises glassy carbon electrodes (5) held with stainless steel clamps (4). A magnetic stirrer bar (6) ensures mixing in the reaction apparatus. A Teflon stopper (2) rests on top of the reaction apparatus, through which stainless steel holders (1) for the electrodes lead.

25 The reaction apparatus, a beaker cell here, has a fitted outlet (3) for a reflux condenser attachment.

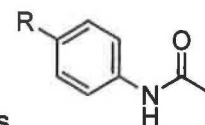


Figure 2: E_{ox} as a function of the *para* substituents of acetanilides

In general, through addition of methanol, a rise in E_{ox} of 4-substituted acetanilides is observed. It is noticeable here that E_{ox} of 4-methoxyacetanilide on addition of about 8% by volume of MeOH is actually raised above E_{ox} of 4-*tert*-butylacetanilide. A rise in E_{ox} by up to 100 mV is possible in a selective manner.

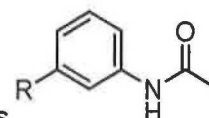


Figure 3: E_{ox} as a function of the *meta* substituents of acetanilides

10

The addition of methanol to *meta*-substituted acetanilides, shown here using the example of 3-methoxyacetanilide, leads to a virtually linear decrease in E_{ox} . A drop of 80 mV has been measured here.

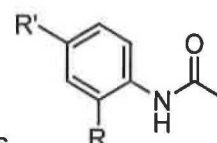


Figure 4: E_{ox} as a function of the *ortho,para* disubstitution of acetanilides

15

The changes in E_{ox} in the case of 2,4 disubstitution only have a weak effect on acetanilides. Only a slight rise ($R = R' = \text{Me}$) or drop ($R = \text{Me}$, $R' = \text{Cl}$) in E_{ox} can be observed. Addition of methanol in the case of this substitution pattern causes a variation in the oxidation potentials by about 30 mV.

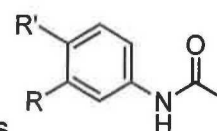


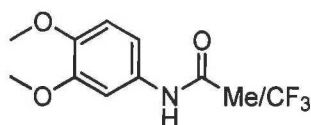
Figure 5: E_{ox} as a function of the *meta,para* disubstitution of acetanilides

20

In contrast, a significant lowering in E_{ox} is possible when using a 3,4 disubstitution. It is found here that the substrate having the higher electron density (a benzodioxole derivative) experiences a distinct drop by almost 300 mV.

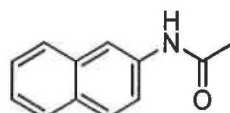
25

Figure 6: Comparison of E_{ox} as a function of the protection of 3,4-dimethoxyaniline



The use of trifluoroacetyl rather than acetyl protecting groups, as a result of strong electron withdrawal by the fluorine atoms, causes a rise in E_{ox} of 3,4-dimethoxyaniline by about 150 mV. At the same time, the influence of MeOH on the trifluoroacetyl derivative is considerably enhanced. The latter derivative, in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), experiences a drop of up to 250 mV in the case of addition of MeOH.

Figure 7: E_{ox} as a function of *N*-(naphthalen-2-yl)acetamide



N-(Naphthalen-2-yl)acetamide shows a similar plot to *p*-methoxyacetanilide. Addition of methanol results in a distinct rise in E_{ox} to about 15% by volume. A shift of about 140 mV is possible in this way. In the case of greater amounts of MeOH, there is a drop in E_{ox} here too.

On the basis of the results shown in Figures 2-7, it becomes clear that the oxidation potentials can be influenced by the different protecting groups and hence the electrochemical coupling can be controlled.

Analysis

Chromatography

The preparative liquid chromatography separations via flash chromatography were conducted with a maximum pressure of 1.6 bar on 60 M silica gel (0.040-0.063 mm) from Macherey-Nagel GmbH & Co, Düren. The unpressurized separations were conducted on Geduran Si 60 silica gel (0.063-0.200 mm) from Merck KGaA, Darmstadt. The solvents used as eluents (ethyl acetate (technical grade), cyclohexane (technical grade)) had been purified by distillation beforehand on a rotary evaporator.

For thin-film chromatography (TLC), ready-made PSC silica gel 60 F254 plates from Merck KGaA, Darmstadt were used. The R_f values are reported as a function of the eluent mixture

used. The TLC plates were stained using a cerium/molybdatophosphoric acid solution as immersion reagent. Cerium/molybdatophosphoric acid reagent: 5.6 g of molybdatophosphoric acid, 2.2 g of cerium(IV) sulphate tetrahydrate and 13.3 g of concentrated sulphuric acid to 200 ml of water.

5

Gas chromatography (GC/GCMS)

The gas chromatography studies (GC) on product mixtures and pure substances were effected with the aid of the GC-2010 gas chromatograph from Shimadzu, Japan. Analysis is effected on an HP-5 quartz capillary column from Agilent Technologies, USA (length: 30 m; internal diameter: 0.25 mm; film thickness of the covalently bound stationary phase: 0.25 μ m; carrier gas: hydrogen; injector temperature: 250°C; detector temperature: 310°C; program: "hard" method: start temperature 50°C for 1 min, heating rate: 15°C/min, end temperature 290°C for 8 min). Gas chromatography mass spectra (GC-MS) of product mixtures and pure substances were taken with the aid of the GC-2010 gas chromatograph combined with the GCMS-QP2010

15 mass detector from Shimadzu, Japan. Analysis is effected on an HP-1 quartz capillary column from Agilent Technologies, USA (length: 30 m; internal diameter: 0.25 mm; film thickness of the covalently bound stationary phase: 0.25 μ m; carrier gas: hydrogen; injector temperature: 250°C; detector temperature: 310°C; program: "hard" method: start temperature 50°C for 1 min, heating rate: 15°C/min, end temperature 290°C for 8 min; GC-MS: ion source temperature: 200°C).

20

Melting points

Melting points were measured with the aid of the SG 2000 melting point determination instrument from HW5, Mainz, and are uncorrected.

25 Elemental analysis

The elemental analyses were conducted in the analytical division of the Organic Chemistry department of the Johannes Gutenberg University of Mainz on a Vario EL Cube from Foss-Heraeus, Hanau.

30 Mass spectrometry

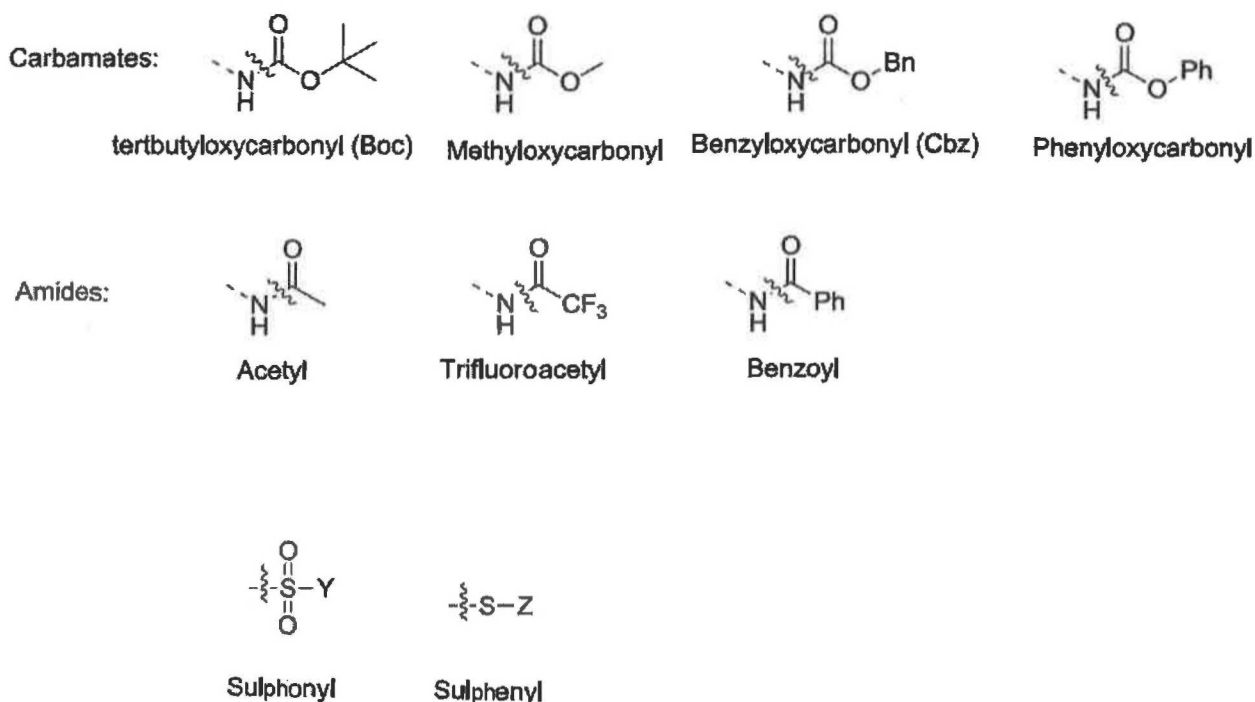
All electrospray ionization analyses (ESI+) were conducted on a QToF Ultima 3 from Waters Micromasses, Milford, Massachusetts. EI mass spectra and the high-resolution EI spectra were analysed on an instrument of the MAT 95 XL sector field instrument type from ThermoFinnigan, Bremen.

NMR spectroscopy

The NMR spectroscopy studies were conducted on multi-nucleus resonance spectrometers of the AC 300 or AV II 400 type from Bruker, Analytische Messtechnik, Karlsruhe. The solvent used was CDCl₃. The ¹H and ¹³C spectra were calibrated according to the residual content of undeuterated solvent using the NMR Solvent Data Chart from Cambridge Isotopes Laboratories, USA. Some of the ¹H and ¹³C signals were assigned with the aid of H,H-COSY, H,H-NOESY, H,C-HSQC and H,C-HMBC spectra. The chemical shifts are reported as δ values in ppm. For the multiplicities of the NMR signals, the following abbreviations were used: s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets), tq (triplet of quartets). All coupling constants J were reported in hertz (Hz) together with the number of bonds covered. The numbering given in the assignment of signals corresponds to the numbering shown in the formula schemes, which do not necessarily have to correspond to IUPAC nomenclature.

15

Examples of possible protecting groups:



20 with Bn = benzyl, Ph = phenyl.

The Y and Z radicals correspond to the definition given above.

The introduction of the protecting groups can be effected, for example, as described in P. G. M. Wuts, T. W. Greene "Greene's Protective Groups in Organic Synthesis", fourth edition, 2007, John Wiley and Sons; Hoboken, New Jersey.

5

M1: Method for N-acetylation

The aniline derivative or naphthylamine derivative to be protected (1 equiv.) is initially charged in a round-neck flask and dissolved in dichloromethane. While cooling with ice, 1.2 equiv. of acetic anhydride are gradually added dropwise to the reaction solution. On completion of
10 addition, the reaction mixture is stirred at room temperature and/or under reflux for 24 hours. After the reaction has ended, the solvent is removed under reduced pressure and the crude product is purified by flash chromatography on silica gel 60 in the eluent CH:EA (4:1 to 1:1).

M2: Method for N-2,2,2-trifluoroacetamide protection

15 A round-neck flask is initially charged with the aniline derivative or naphthylamine derivative to be protected (1 equiv.) in dichloromethane solution. While cooling with ice and stirring vigorously, 1.2 equiv. of trifluoroacetic anhydride are added gradually to this solution. After the addition has ended, the reaction flask is heated to 35°C for 4-5 hours. After the reaction has ended, the solvent is removed under reduced pressure and the crude product is purified by
20 flash chromatography on silica gel 60 in the eluent CH:EA (4:1 to 1:1).

M3: Method for electrochemical cross-coupling

In an undivided beaker cell having glassy carbon electrodes, 3.8 mmol of component **A** (cf. Reaction Scheme 2) and 7.6 mmol of component **B** to be coupled (cf. Reaction Scheme 2) are
25 dissolved in 25 ml of 1,1,1,3,3,3-hexafluoroisopropanol and 0.77 g of MTBS. The electrolysis is galvanostatic. During the electrolysis, the beaker cell is heated to 50°C with the aid of a water bath and the reaction mixture is stirred. After the electrolysis has ended, the cell contents are transferred to a corresponding round-neck flask and the solvent is removed on a rotary
evaporator at 50°C, 200 → 90 mbar, under reduced pressure.

30

Electrode material:

Anode: glassy carbon

Cathode: glassy carbon

Electrolysis conditions:

Temperature [T]: 50°C

Current density [j]: 2.8 mA/cm²

Charge [Q]: 2 F (per deficiency component)

5

M4: Method for electrochemical cross-coupling (screening)

In an undivided screening cell, 0.76 mmol of component **A** (cf. Reaction Scheme 2) and 1.51 mmol of component **B** to be coupled (cf. Reaction Scheme 2) were dissolved in 5 ml of 1,1,1,3,3,3-hexafluoroisopropanol and 154 mg of MTBS. The electrolysis is galvanostatic.

- 10 During the electrolysis, the screening cell is heated to 50°C in a screening block and the reaction mixture is stirred. After the electrolysis has ended, the cell contents are transferred to a corresponding round-neck flask and the solvent is removed on a rotary evaporator at 50°C, 200 → 90 mbar, under reduced pressure.

- 15 Electrode material:

Anode: BDD or glassy carbon

Cathode: BDD or glassy carbon

Electrolysis conditions:

- 20 Temperature [T]: 50°C

Current density [j]: 2.8 mA/cm²

Charge [Q]: 2 F (per deficiency component)

M5: General method for removal of N-2,2,2-trifluoroacetamide protecting groups

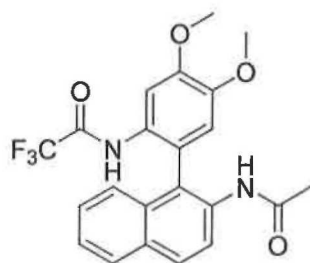
- 25 A round-neck flask is initially charged with 1 equiv. of the substrate to be deprotected, dissolved in a methanol/water mixture in a ratio of 2:1. Then 10 equiv. of potassium carbonate are added to the reaction solution, which is stirred at room temperature for four days. After the reaction has ended, the solvent is removed under reduced pressure. The residue is slurried with water and the deprotected product is extracted with dichloromethane. Unless deprotection is quantitative,
- 30 the crude product is purified by flash chromatography on silica gel 60.

M6: General method for removal of N-acetyl protecting groups

The substrate to be deprotected (1 equiv.) is initially charged in a round-neck flask and dissolved in methanol. While stirring vigorously, 12 equiv. of boron trifluoride diethyl etherate

are added to the reaction solution, and then the mixture is heated under reflux for 18 hours. The reaction is ended by addition of 20 equiv. of triethylamine, and the product which precipitates out in solid form can be filtered off.

5 2-(N-Acetyl)amino-1-(2'-(N'-trifluoroacetyl)amino-4',5'-dimethoxyphenyl)naphthalene



a) Synthesis of 2,2'-diaminobiaryl on the screening scale

The electrolysis is conducted according to **M4** in an undivided screening cell. For this purpose,
 10 140 mg (0.76 mmol, 1.0 equiv.) of N-(naphthalen-2-yl)acetamide and 377 mg (1.51 mmol, 2 equiv.) of N-(3,4-dimethoxyphenyl)-2,2,2-trifluoroacetamide are dissolved in 5 ml of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), 154 mg of MTBS are added and the electrolyte is transferred into the electrolysis cell. After the electrolysis, the solvent and unconverted reactants are removed under reduced pressure. The crude product is then purified by flash chromatography on silica
 15 gel 60 in a 2:1 eluent (CH:EA), and the product is obtained as a colourless solid.

The screening reaction was used to examine different electrode materials. The electrode materials used were chosen BDD and glassy carbon, which prepared the C,C cross-coupling product in different yields (Table 1).

20

Table 1: List of the electrode materials used with the resulting yields

Electrode material	Yield
BDD	24% (78 mg)
glassy carbon	44% (144 mg)

Electrode material	Yield
25 BDD	24% (78 mg)
Glassy carbon	44% (144 mg)

b) Synthesis of 2,2'-diaminobiaryl in a beaker cell

The electrolysis is conducted according to **M3** in an undivided beaker cell with glassy carbon electrodes. 0.70 g (3.79 mmol, 1.0 equiv.) of N-(naphthalen-2-yl)acetamide and 1.89 g (7.57 mmol, 2 equiv.) of N-(3,4-dimethoxyphenyl)-2,2,2-trifluoroacetamide are dissolved in 25 ml of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), 0.77 g of MTBS are added and the electrolyte is transferred into the electrolysis cell. The solvent and unconverted amounts of reactant are removed under reduced pressure after the electrolysis, the crude product is purified by flash chromatography on silica gel 60 in a 2:1 eluent (CH:EA) and the product is obtained as a colourless solid.

10

Yield: 1.02 g (62%, 2.36 mmol)

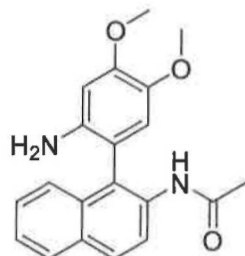
GC (hard method, HP-5): tR = 16.90 min

Rf (EA:CH = 2:1) = 0.5

¹H NMR (300 MHz, CDCl₃) δ = 2.00 (s, 3H), 3.84 (s, 3H), 4.01 (s, 3H), 6.73 (s, 1H), 7.15 (bs, 1H), 7.27 (d, J = 9 Hz, 1H), 7.44 (dt, J = 6 Hz, 1H), 7.66 (s, 1H), 7.91 (m, 3H) 7.93 (bs, 1H), 8.11 (d, 1H)

¹³C NMR (75 MHz, CDCl₃) δ = 24.23, 56.33, 56.38, 107.73, 113.15, 113.63, 117.45, 120.79, 122.57, 124.55, 124.88, 125.96, 127.03, 127.54, 128.47, 130.08, 131.51, 132.36, 133.98, 148.10, 149.53, 169.47

HRMS for C₂₂H₁₉F₃N₂O₄ (ESI⁺) [M+H⁺]: calc.: 433.1375, found: 433.1375

2-(N-Acetyl)amino-1-(2'-amino-4',5'-dimethoxyphenyl)naphthalene

25

In a round-neck flask, according to **M5**, 0.65 g (1.50 mmol, 1 equiv.) of 2-(N-acetyl)amino-1-(2'-(N'-trifluoroacetyl)-amino-4',5'-dimethoxyphenyl)naphthalene is dissolved in 120 ml of a methanol/water mixture in a ratio of 2:1. 2.07 g (15.01 mmol, 10 equiv.) of potassium carbonate are added to this solution and the reaction mixture is stirred at room temperature for four days.

After the reaction has ended, the solvent is removed under reduced pressure, the residue is slurried with water and the deprotected product is extracted with dichloromethane.

Yield: 500 mg (99%, 1.49 mmol)

5 GC (hard method, HP-5): tR = 18.68 min

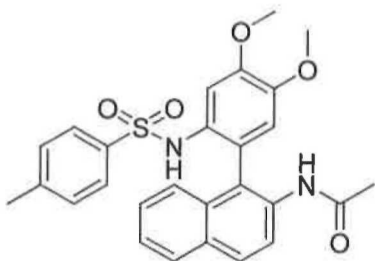
Rf (EA:CH = 2:1) = 0.46

^1H NMR (300 MHz, CDCl_3) δ = 2.03 (s, 3H), 3.12 (bs, 2H), 3.77 (s, 3H), 3.94 (s, 3H), 6.59 (d, J = 15 Hz, 2H), 7.35-7.46 (m, 4H), 7.87 (dd, J = 9 Hz, 2H), 8.40 (d, J = 9 Hz, 1H)

10 ^{13}C NMR (75 MHz, CDCl_3) δ = 24.87, 56.02, 56.58, 101.21, 111.55, 114.60, 121.36, 123.50, 125.18, 125.61, 126.81, 128.25, 129.01, 131.28, 132.77, 134.48, 137.70, 143.04, 150.28, 168.96

HRMS for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_3$ (ESI+) [M+H] $^+$: calc.: 337.1552, found: 337.1552

15 2-(N-Acetyl)amino-1-(2'-(N'-(4-methylphenylsulphonyl))amino-4',5'-dimethoxyphenyl)naphthalene



278 mg (0.83 mmol, 1 equiv.) of N-acetyl-2-amino-1-(2'-amino-4',5'-dimethoxyphenyl)naphthalene in 110 ml of dichloromethane are initially charged in a round-bottom flask. Added to this reaction solution are 173 mg (0.91 mmol, 1.1 equiv.) of p-methylsulphonyl chloride and 0.13 ml (0.91 mmol, 1.1 equiv.) of triethylamine, and the mixture is stirred at room temperature for 111 hours. After the reaction has ended, the solvent is removed under reduced pressure and the crude product is purified by flash chromatography on silica gel 60 in a 2:1 eluent (CH:EA).

25

Yield: 342 mg (84 %, 0.70 mmol)

GC (hard method, HP-5): tR = 16.87 min

Rf (EA:CH = 2:1) = 0.21

30 ^1H NMR (300 MHz, CDCl_3) δ = 1.87 (s, 3H), 2.38 (s, 3H), 3.75 (s, 3H), 3.94 (s, 3H), 6.09 (s, 1H), 6.56 (s, 1H), 6.68 (s, 1H), 6.94 (d, J = 9 Hz, 1H), 7.10 (d, J = 6 Hz, 2H), 7.24 (t, J = 6 Hz,

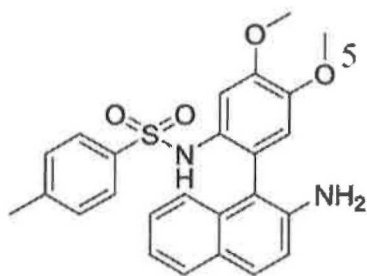
1H), 7.29 (bs, 1H), 7.36 (d, J = 9 Hz, 2H), 7.42 (t, J = 6 Hz, 1H), 7.88 (dd, J = 15 Hz, J = 9 Hz, 2H), 8.32 (d, J = 9 Hz, 1H)

¹³C NMR (75 MHz, CDCl₃) δ = 21.70, 24.58, 56.19, 56.27, 106.87, 113.17, 119.35, 121.46, 124.49, 124.89, 125.40, 125.92, 127.40, 127.40, 127.44, 128.50, 129.74, 129.74, 129.81,

5 130.98, 132.28, 134.61, 136.40, 144.15, 147.38, 149.75, 168.58

HRMS for C₂₀H₂₀N₂O₃ (ESI⁺) [M+H⁺]: calc.: 491.1641, found: 491.1651

2-Amino-1-(2'-N-(4-methylphenylsulphonyl)-amino-4',5'-dimethoxyphenyl)naphthalene



- 10 According to **M6**, 342 mg (0.70 mmol, 1 equiv.) of N-acetyl-2-amino-1-(2'-N-(4-methylphenylsulphonyl)-amino-4',5'-dimethoxyphenyl)naphthalene are initially charged in 40 ml of methanol. 1.06 ml (8.37 mmol, 12 equiv.) of boron trifluoride diethyl etherate are added to this solution while stirring vigorously, and the mixture is heated under reflux for 18 hours. The reaction is ended by the addition of 2 ml of triethylamine, and the product which precipitates out
- 15 in solid form can be filtered off.

Yield: 219 mg (70 %, 0.49 mmol)

GC (hard method, HP-5): tR = 15.64 min

Rf (EA:CH = 2:1) = 0.78

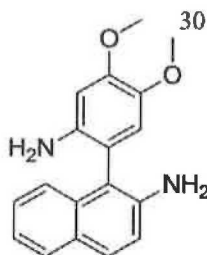
- 20 ¹H NMR (300 MHz, CDCl₃) δ = 2.21 (s, 3H), 3.00 (bs, 2H), 3.76 (s, 3H), 3.98 (s, 3H), 6.64 (s, 1H), 6.73-6.83 (m, 4H), 7.00-7.08 (m, 2H), 7.15-7.24 (m, 3H), 7.40 (s, 1H), 7.70 (dd, J = 6 Hz, J = 9 Hz, 2H)

¹³C NMR (75 MHz, CDCl₃) δ = 21.61, 56.18, 56.27, 108.18, 114.19, 114.95, 118.02, 120.61, 122.65, 123.75, 126.88, 126.98, 126.98, 128.08, 128.34, 128.49, 129.25, 129.25, 130.04,

- 25 133.51, 135.97, 140.54, 143.28, 147.20, 149.30

HRMS for C₂₀H₂₀N₂O₃ (ESI⁺) [M+H⁺]: calc.: 449.1535, found: 449.1542

2-Amino-1-(2'-N-(4-methylphenylsulphonyl)-amino-4',5'-dimethoxyphenyl)naphthalene



In a round-neck flask, 300 mg (0.69 mmol, 1 equiv.) of 2-(N-acetyl)amino-1-(2'-(N'-trifluoroacetyl)-amino-4',5'-dimethoxyphenyl)naphthalene are dissolved in 80 ml of hydrazine hydrate solution (80% aqueous solution). The reaction solution is stirred under reflux at 120°C for 4 days. After the reaction has ended, the mixture is extracted 3 times with 20 ml of dichloromethane each time, and the solvent is removed under reduced pressure. The product is obtained as a brownish foam.

Yield: 200 mg (98%, 0.68 mmol)

GC (hard method, HP-5): tR = 17.21 min

Rf (EA:CH = 2:1) = 0.44

^1H NMR (300 MHz, CDCl_3) δ = 3.61 (s, 3H), 3.77 (s, 3H), 4.01 (bs, 2H), 4.77 (bs, 2H), 6.50 (s, 1H), 6.58 (s, 1H), 7.09-7.25 (m, 4H), 7.66 (d, J = 9 Hz, 1H), 7.69 (d, J = 6 Hz, 1H)

^{13}C NMR (75 MHz, CDCl_3) δ = 55.25, 56.37, 100.60, 111.34, 113.66, 116.07, 118.46, 120.99,

123.45, 125.97, 127.07, 127.88, 128.19, 133.70, 140.43, 140.84, 143.58, 149.32

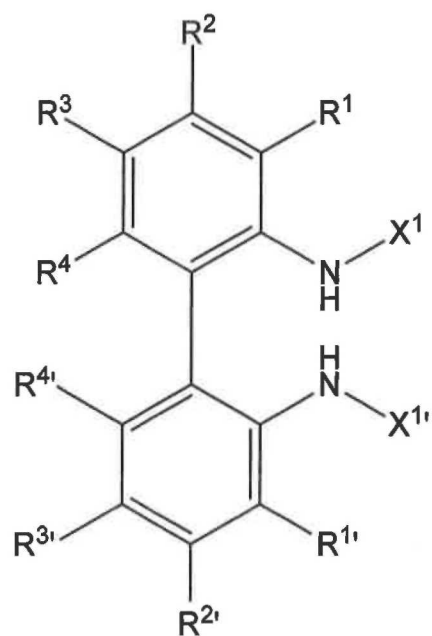
HRMS for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_2$ (ESI+) $[\text{M}+\text{H}^+]$: calc.: 295.1447, found: 295.1458

The compounds shown in the examples solve the stated problem. It has been possible for the first time to prepare novel 2,2'-diaminobiaryls in good to very good yields. At the same time, an entirely novel synthesis strategy is employed: Both aminoaryls are first protected independently, then electrochemically coupled, and can then be selectively deprotected if required. Through this procedure, it is possible to prepare compound having two different protecting groups which were unobtainable because of the existing procedure specified in the prior art.

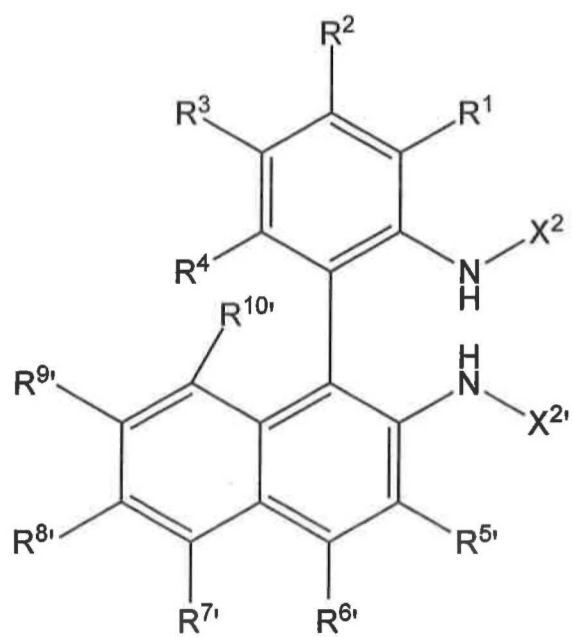
Claims

1. Compound having one of the general structures (I) to (III):

5

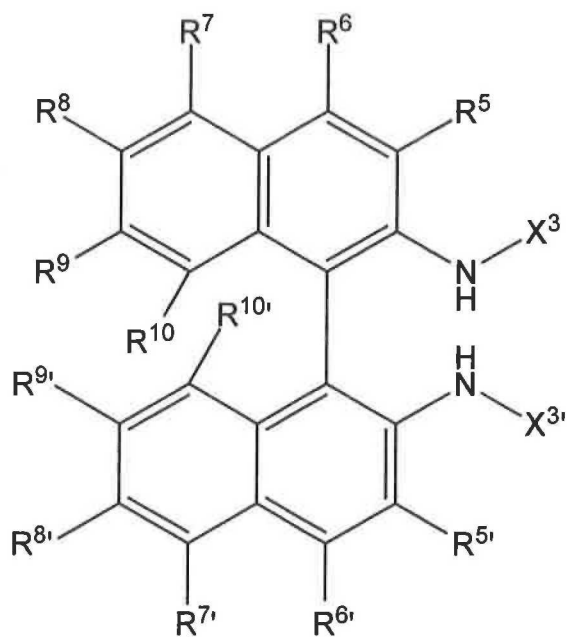


(I)



(II)

10



(III)

5

where

$R^1, R^2, R^3, R^4, R^{1'}, R^{2'}, R^{3'}, R^{4'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen, -COO-(C₁-C₁₂)-alkyl, -CONH-(C₁-C₁₂)-alkyl, -CO-(C₁-C₁₂)-alkyl, -CO-(C₆-C₂₀)-aryl, -COOH, -OH, -SO₃H, -CN, -N[(C₁-C₁₂)-alkyl]₂;

10

$R^5, R^6, R^7, R^8, R^9, R^{10}, R^{5'}, R^{6'}, R^{7'}, R^{8'}, R^{9'}, R^{10'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen, -COO-(C₁-C₁₂)-alkyl, -CONH-(C₁-C₁₂)-alkyl, -CO-(C₁-C₁₂)-alkyl, -CO-(C₆-C₂₀)-aryl, -COOH, -OH, -SO₃H, -N[(C₁-C₁₂)-alkyl]₂;

15

where the alkyl and aryl groups mentioned may be substituted;

X^1 and $X^{1'}$ are selected from:

tert-butoxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl, and X^1 is not the same radical as $X^{1'}$;

20

and the following two radical pairs are excluded:

X^1 = acetyl and $X^{1'}$ = benzoyl,

X^1 = benzoyl and $X^{1'}$ = acetyl;

X^2 and $X^{2'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl,
and X^2 is not the same radical as $X^{2'}$;

X^3 and $X^{3'}$ are selected from:

- 5 *tert*-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl,
and X^3 is not the same radical as $X^{3'}$.

2. Compound according to Claim 1,

- 10 where X^1 and $X^{1'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

3. Compound according to either of Claims 1 and 2,

- 15 where X^2 and $X^{2'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

4. Compound according to any of Claims 1 to 3,

- 20 where X^3 and $X^{3'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl.

5. Compound according to any of Claims 1 to 4,

- 25 where $R^1, R^2, R^3, R^4, R^{1'}, R^{2'}, R^{3'}, R^{4'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen.

6. Compound according to any of Claims 1 to 5,

where $R^1, R^2, R^3, R^4, R^{1'}, R^{2'}, R^{3'}, R^{4'}$ are selected from:

- 30 -H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl.

7. Compound according to any of Claims 1 to 6,

where $R^{5'}, R^{6'}, R^{7'}, R^{8'}, R^{9'}, R^{10'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen.

8. Compound according to any of Claims 1 to 7,
 where R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} are selected from:
 -H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl.

5

9. Compound according to any of Claims 1 to 8,
 where R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} are selected from:
 -H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen.

10 10. Compound according to any of Claims 1 to 9,
 where R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} are selected from:
 -H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl.

11. Compound according to any of Claims 1 to 10,
 15 wherein the compound has one of the two general structures (I) and (II).

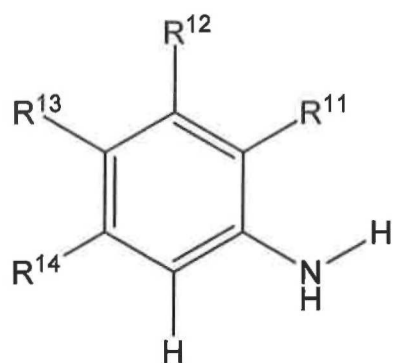
12. Compound according to any of Claims 1 to 11,
 wherein the compound has the general structure (I).

20 13. Compound according to any of Claims 1 to 11,
 wherein the compound has the general structure (II).

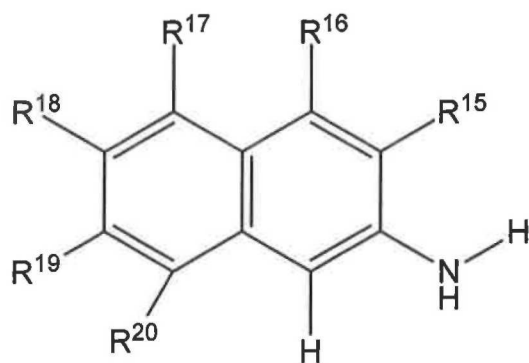
14. Compound according to any of Claims 1 to 10,
 wherein the compound has the general structure (III).

25

15. Process for preparing 2,2'-diaminobiaryls, comprising the process steps of:
 a) reacting a compound of the formula (IVa) or (Va):

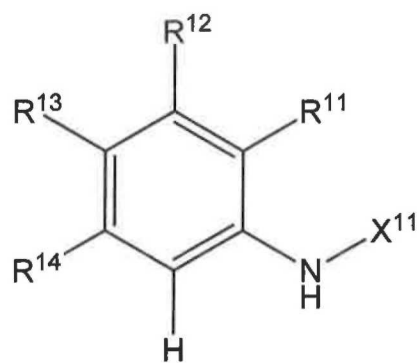


(IVa)

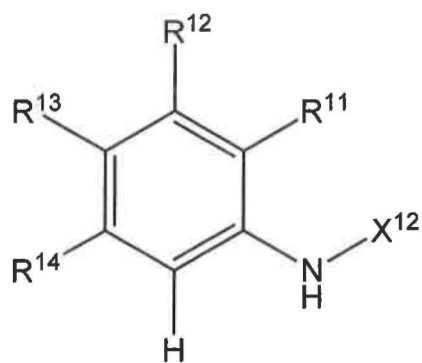


(Va)

- 5 with reaction of (IVa) with X^{11} or X^{12} to give (IVb1) or (IVb2), or of (Va) with X^{13} to give (Vb):

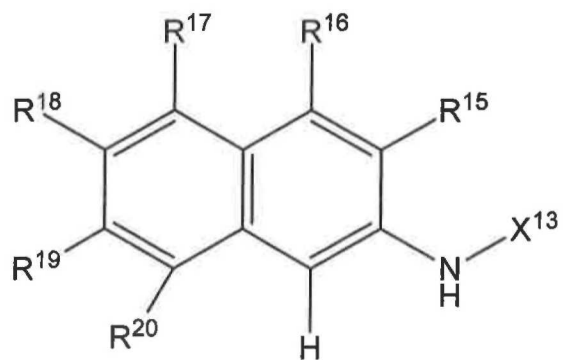


(IVb1)



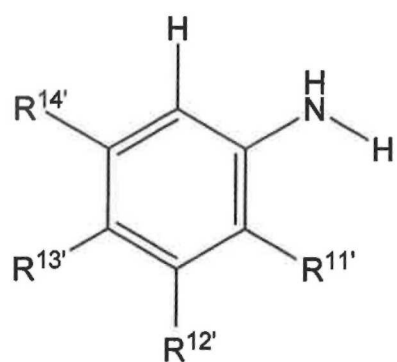
(IVb2)

10

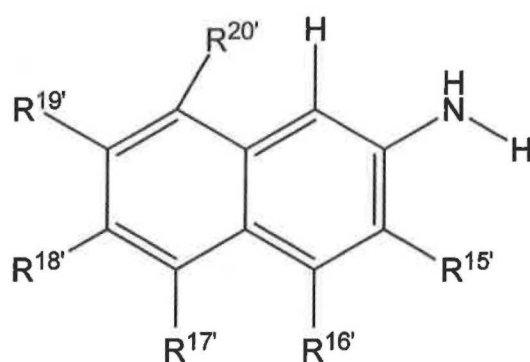


(Vb)

- 15 b) reacting a compound of the formula (VIa) or (VIIa):



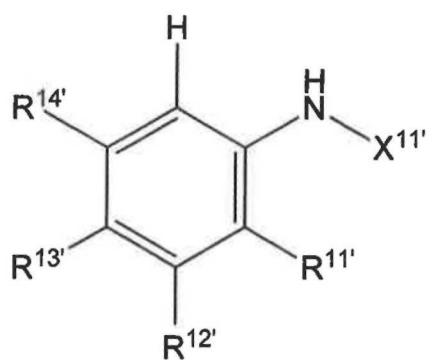
(VIa)



(VIIa)

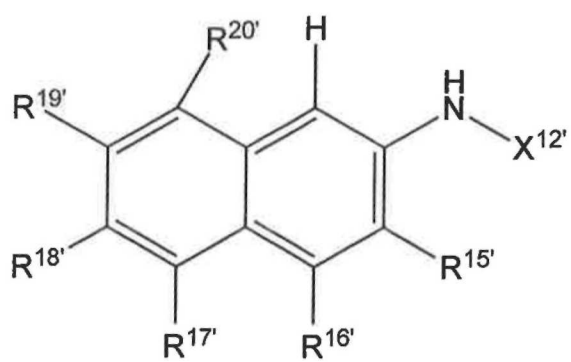
5

with reaction of (VIa) with $X^{11'}$ to give (VIb), or
of (VIIa) with $X^{12'}$ or $X^{13'}$ to give (VIIb1) or (VIIb2):



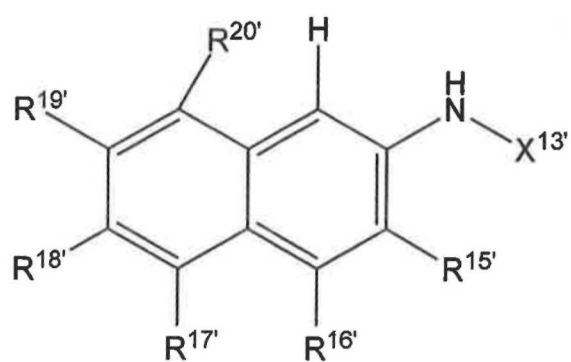
(VIb)

10



(VIIb1)

15

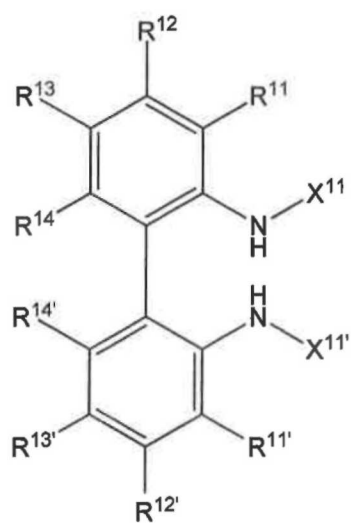


(VIIb2)

c) electrochemical coupling of:

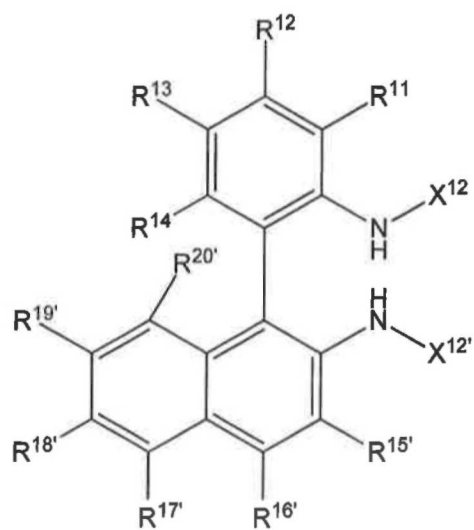
- (IVb1) with (VIb) to give (I*), or
 - (IVb2) with (VIIb1) to give (II*), or
- 5 - (Vb) with (VIIb2) to give (III*),

in each case with use of the compound having the higher oxidation potential in excess:

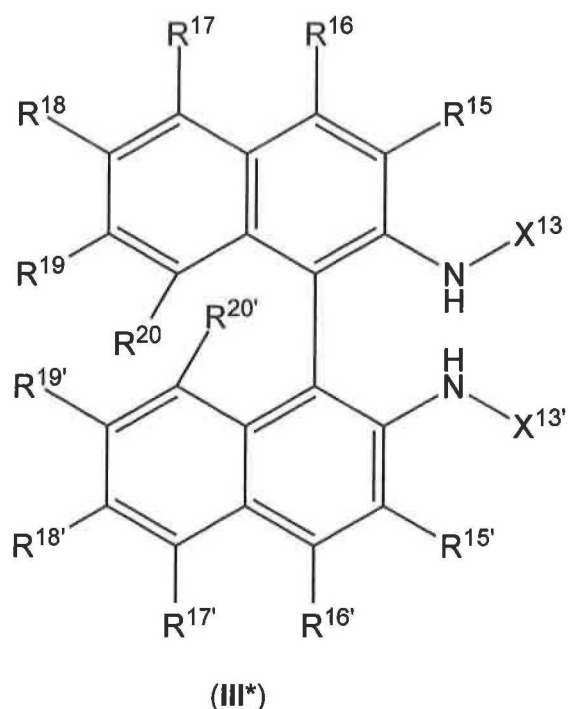


10

(I*)



(II*)



5

where

R^{11} , R^{12} , R^{13} , R^{14} , $R^{11'}$, $R^{12'}$, $R^{13'}$, $R^{14'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen, -COO-(C₁-C₁₂)-alkyl, -CONH-(C₁-C₁₂)-alkyl, -CO-(C₁-C₁₂)-alkyl, -CO-(C₆-C₂₀)-aryl, -COOH, -OH, -SO₃H, -CN, -N[(C₁-C₁₂)-alkyl]₂;

10

R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} , $R^{15'}$, $R^{16'}$, $R^{17'}$, $R^{18'}$, $R^{19'}$, $R^{20'}$ are selected from:

-H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl, -S-alkyl, -S-aryl, halogen, -COO-(C₁-C₁₂)-alkyl, -CONH-(C₁-C₁₂)-alkyl, -CO-(C₁-C₁₂)-alkyl, -CO-(C₆-C₂₀)-aryl, -COOH, -OH, -SO₃H, -N[(C₁-C₁₂)-alkyl]₂;

15

where the alkyl and aryl groups mentioned may be substituted;

X^{11} and $X^{11'}$ are selected from:

tert-butoxycarbonyl, methoxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl, and X^{11} is not the same radical as $X^{11'}$;

20

X^{12} and $X^{12'}$ are selected from:

tert-butoxycarbonyl, methoxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl, and X^{12} is not the same radical as $X^{12'}$;

X^{13} and $X^{13'}$ are selected from:

tert-butyloxycarbonyl, methyloxycarbonyl, benzyloxycarbonyl, phenyloxycarbonyl, acetyl, trifluoroacetyl, benzoyl, sulphonyl, sulphenyl, and X^{13} is not the same radical as $X^{13'}$.