

Electrochemical method for coupling phenol to aniline

The present invention relates to an electrochemical process for coupling of phenol to aniline.

- 5 The terms “anilines” and “phenols” are used in this application as generic terms and thus encompass substituted aminoaryls and substituted hydroxyaryls.

The direct cross-coupling of unprotected phenol and aniline derivatives is known to date only by a conventional organic route and for very few examples. Here, principally superstoichiometric
10 amounts of inorganic oxidizing agents such as Cu(II) (see: M. Smrcina, M. Lorenc, V. Hanus, P. Kocovsky, *Synlett*, **1991**, 4, 231, M. Smrcina, S. Vyskocil, B. Maca, M. Polasek, T. A. Claxton, A. P. Abbott, P. Kocovsky, *J. Org. Chem.* **1994**, 59, 2156, M. Smrcina, M. Lorenc, V. Hanus, P. Sedmera, P. Kocovsky, *J. Org. Chem.* **1992**, 57, 191, M. Smrcina, J. Polakova, S. Vyskocil, P. Kocovsky, *J. Org. Chem.* **1993**, 58, 4534) or Fe(III) (see: K. Ding, Q. Xu, Y. Wang, J. Liu, Z. Yu,
15 B. Du, Y. Wu, H. Koshima, T. Matsuura, *Chem. Commun.* **1997**, 7, 693, S. Vyskocil, M. Smrcina, M. Lorenc, P. Kocovsky, V. Hanus, M. Polasek, *Chem. Commun.* **1998**, 5, 585) were utilized.

In rare cases, cross-coupling is possible by means of oxygen as an oxidizing agent when
20 vanadium catalysts are used, as in S.-W. Hon, C.-H. Li, J.-H. Kuo, N. B. Barhate, Y.-H. Liu, Y. Wang, C.-T. Chen, *Org. Lett.* **2001**, 3, 869.

Other synthesis routes involved either the protection of the amino group from the oxidative cross-coupling with transition metal catalysts or the subsequent introduction of these functional
25 groups into the biaryl base skeleton (see R. A. Singer, S. L. Buchwald, *Tetrahedron Letters*, **1999**, 40, 1095, K. Körber, W. Tang, X. Hu, X. Zhang, *Tetrahedron Letters*, **2002**, 43, 7163, E. P. Studentsov, O. V. Piskunova, A. N. Skvortsov, N. K. Skvortsov, *Russ. J. Gen. Chem.* **2009**, 79, 962, D. Sälinger, R. Brückner, *Synlett*, **2009**, 1, 109)

30 A great disadvantage of the abovementioned methods for phenol-aniline cross-coupling is the frequent necessity for dry solvents and exclusion of air. In addition, large amounts of oxidizing agents, some of them toxic, are often used. During the reaction, toxic by-products often occur, which have to be separated from the desired product in a costly and inconvenient manner and disposed of at great cost. As a result of increasingly scarce raw materials (for example boron

and bromine in the case of transition metal-catalysed cross-coupling) and the rising relevance of environmental protection, the cost of such transformations is rising. Particularly in the case of utilization of multistage sequences, an exchange between various solvents is necessary.

A problem which 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 drive to release an electron (e^-) to the anode and a H^+ ion to the solvent, for example, than the molecule having the higher 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 the literature methods cited above were to be applied to two different substrates, the result of this would be to form predominantly radicals of the molecule having a lower oxidation potential, and these would then react with one another. By far the predominant main product obtained would thus be a product which has formed from two identical substrates.

This problem does not occur in the coupling of identical molecules.

The problem addressed by the present invention was that of providing an electrochemical process in which anilines and phenols can be coupled to one another, and multistage syntheses using metallic reagents can be dispensed with.

The problem is solved by a process according to the invention.

Summary

In one embodiment, there is provided an electrochemical process for coupling phenol to aniline, comprising the process steps of:

- a') introducing a solvent or solvent mixture and a conductive salt into a reaction vessel,
- b') adding a phenol having an oxidation potential E_{Ox1} to the reaction vessel,

c') adding an aniline having an oxidation potential E_{Ox2} to the reaction vessel, where:

$$E_{Ox2} > E_{Ox1} \quad \text{and} \quad E_{Ox2} - E_{Ox1} = \Delta E,$$

the aniline being added in excess relative to the phenol,

and the solvent or solvent mixture being selected such that ΔE is within the range from 10 mV to 450 mV,

d') introducing two electrodes into the reaction solution,

e') applying a voltage to the electrodes,

f') coupling the phenol and the aniline.

In one aspect, there is provided an electrochemical process for coupling phenol to aniline, comprising the process steps of:

a'') introducing a solvent or solvent mixture and a conductive salt into a reaction vessel,

b'') adding an aniline having an oxidation potential E_{Ox1} to the reaction vessel,

c'') adding a phenol having an oxidation potential E_{Ox2} to the reaction vessel, where:

$$E_{Ox2} > E_{Ox1} \quad \text{and} \quad E_{Ox2} - E_{Ox1} = \Delta E,$$

the phenol being added in excess relative to the aniline,

and the solvent or solvent mixture being selected such that ΔE is within the range from 10 mV to 450 mV,

d'') introducing two electrodes into the reaction solution,

e'') applying a voltage to the electrodes,

f'') coupling the phenol and the aniline.

Detailed Description

Electrochemical process for coupling phenol to aniline, comprising the process steps of:

a') introducing a solvent or solvent mixture and a conductive salt into a reaction vessel,

b') adding a phenol having an oxidation potential E_{Ox1} to the reaction vessel,

c') adding an aniline having an oxidation potential E_{Ox2} to the reaction vessel, where:

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the aniline being added in excess relative to the phenol,

and the solvent or solvent mixture being selected such that ΔE is within the range from 10 mV to 450 mV,

5 d') introducing two electrodes into the reaction solution,

e') applying a voltage to the electrodes,

f') coupling the phenol and the aniline.

Process steps a) to c) can be effected here in any sequence.

10

Electrochemical process for coupling phenol to aniline, comprising the process steps of:

a'') introducing a solvent or solvent mixture and a conductive salt into a reaction vessel,

b'') adding an aniline having an oxidation potential E_{Ox1} to the reaction vessel,

c'') adding a phenol having an oxidation potential E_{Ox2} to the reaction vessel, where:

$$15 \quad E_{Ox2} > E_{Ox1} \quad \text{and} \quad E_{Ox2} - E_{Ox1} = \Delta E,$$

the phenol being added in excess relative to the aniline,

and the solvent or solvent mixture being selected such that ΔE is within the range from 10 mV to 450 mV,

d'') introducing two electrodes into the reaction solution,

20 e'') applying a voltage to the electrodes,

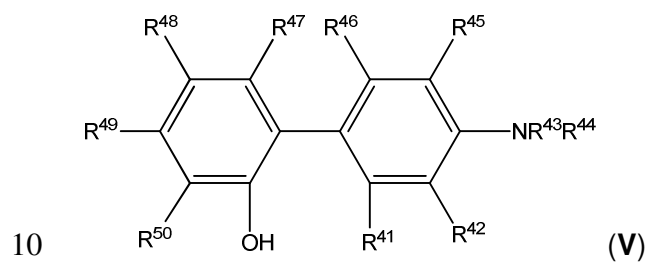
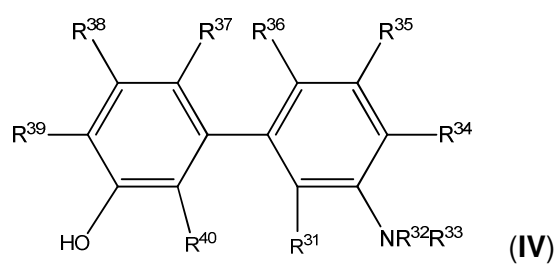
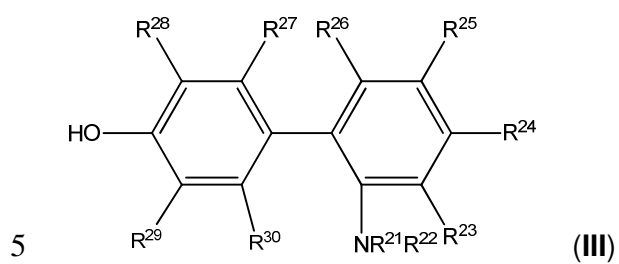
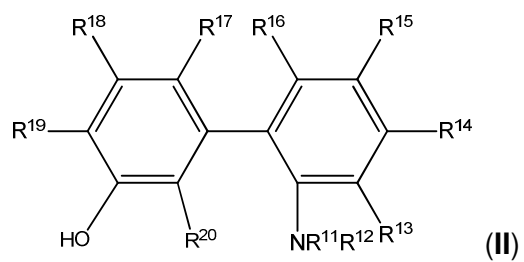
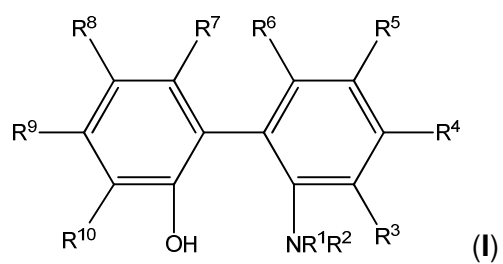
f'') coupling the phenol and the aniline.

Process steps a) to c) can be effected here in any sequence.

25 By electrochemical treatment, phenols are coupled to anilines and the corresponding products are prepared, without needing to add organic oxidizing agents, to work with exclusion of moisture or to observe anaerobic reaction regimes. This direct method of C-C coupling opens up an inexpensive and environmentally friendly alternative to existing multistage synthesis routes conventional in organic synthesis.

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Compounds of one of the general formulae (I) to (V) can be prepared by the process described:



- where the substituents R¹ to R⁵⁰ are each independently selected from the group of hydrogen, hydroxyl, (C₁-C₁₂)-alkyl, (C₁-C₁₂)-heteroalkyl, (C₄-C₁₄)-aryl, (C₄-C₁₄)-aryl-(C₁-C₁₂)-alkyl, (C₄-C₁₄)-aryl-O-(C₁-C₁₂)-alkyl, (C₃-C₁₄)-heteroaryl, (C₃-C₁₄)-heteroaryl-(C₁-C₁₂)-alkyl, (C₃-C₁₂)-cycloalkyl, (C₃-C₁₂)-cycloalkyl-(C₁-C₁₂)-alkyl, (C₃-C₁₂)-heterocycloalkyl, (C₃-C₁₂)-heterocycloalkyl-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-heteroalkyl, O-(C₄-C₁₄)-aryl, O-(C₄-C₁₄)-aryl-(C₁-C₁₄)-alkyl, O-(C₃-C₁₄)-heteroaryl, O-(C₃-C₁₄)-heteroaryl-(C₁-C₁₄)-alkyl, O-(C₃-C₁₂)-cycloalkyl, O-(C₃-C₁₂)-cycloalkyl-(C₁-C₁₂)-alkyl, O-(C₃-C₁₂)-heterocycloalkyl, O-(C₃-C₁₂)-heterocycloalkyl-(C₁-C₁₂)-alkyl, halogens, S-(C₁-C₁₂)-alkyl, S-(C₁-C₁₂)-heteroalkyl, S-(C₄-C₁₄)-aryl, S-(C₄-C₁₄)-aryl-(C₁-C₁₄)-alkyl, S-(C₃-C₁₄)-heteroaryl, S-(C₃-C₁₄)-heteroaryl-(C₁-C₁₄)-alkyl, S-(C₃-C₁₂)-cycloalkyl, S-(C₃-C₁₂)-cycloalkyl-(C₁-C₁₂)-alkyl, S-(C₃-C₁₂)-heterocycloalkyl, (C₁-C₁₂)-acyl, (C₄-C₁₄)-aroyl, (C₄-C₁₄)-aroyl-(C₁-C₁₄)-alkyl, (C₃-C₁₄)-heteroaroyl, (C₁-C₁₄)-dialkylphosphoryl, (C₄-C₁₄)-diarylphosphoryl, (C₃-C₁₂)-alkylsulphonyl, (C₃-C₁₂)-cycloalkylsulphonyl, (C₄-C₁₂)-arylsulphonyl, (C₁-C₁₂)-alkyl-(C₄-C₁₂)-arylsulphonyl, (C₃-C₁₂)-heteroarylsulphonyl, (C=O)O-(C₁-C₁₂)-alkyl, (C=O)O-(C₁-C₁₂)-heteroalkyl, (C=O)O-(C₄-C₁₄)-aryl,
- where the alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl groups mentioned are optionally mono- or polysubstituted.

Alkyl represents an unbranched or branched aliphatic radical.

- Aryl for aromatic (hydrocarbyl) radicals, preferably having up to 14 carbon atoms, for example phenyl (C₆H₅-), naphthyl (C₁₀H₇-), anthryl (C₁₄H₉-), preferably phenyl.

Cycloalkyl for saturated cyclic hydrocarbons containing exclusively carbon atoms in the ring.

- Heteroalkyl for an unbranched or branched aliphatic radical which may contain one to four, preferably one or two, heteroatom(s) selected from the group consisting of N, O, S and substituted N.

- Heteroaryl for an aryl radical in which one to four, preferably one or two, carbon atom(s) may be replaced by heteroatoms selected from the group consisting of N, O, S and substituted N, where the heteroaryl radical may also be part of a larger fused ring structure.

Heterocycloalkyl for saturated cyclic hydrocarbons which may contain one to four, preferably one or two, heteroatom(s) selected from the group consisting of N, O, S and substituted N.

A heteroaryl radical which may be part of a fused ring structure is preferably understood to mean systems in which fused five- or six-membered rings are formed, for example benzofuran, isobenzofuran, indole, isoindole, benzothiophene, benzo(c)thiophene, benzimidazole, purine, indazole, benzoxazole, quinoline, isoquinoline, quinoxaline, quinazoline, cinnoline, acridine.

The substituted N mentioned may be monosubstituted, and the alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl groups may be mono- or polysubstituted, more preferably mono-, di- or trisubstituted, by radicals selected from the group consisting of hydrogen, (C₁-C₁₄)-alkyl, (C₁-C₁₄)-heteroalkyl, (C₄-C₁₄)-aryl, (C₄-C₁₄)-aryl-(C₁-C₁₄)-alkyl, (C₃-C₁₄)-heteroaryl, (C₃-C₁₄)-heteroaryl-(C₁-C₁₄)-alkyl, (C₃-C₁₂)-cycloalkyl, (C₃-C₁₂)-cycloalkyl-(C₁-C₁₄)-alkyl, (C₃-C₁₂)-heterocycloalkyl, (C₃-C₁₂)-heterocycloalkyl-(C₁-C₁₄)-alkyl, CF₃, halogen (fluorine, chlorine, bromine, iodine), (C₁-C₁₀)-haloalkyl, hydroxyl, (C₁-C₁₄)-alkoxy, (C₄-C₁₄)-aryloxy, O-(C₁-C₁₄)-alkyl-(C₄-C₁₄)-aryl, (C₃-C₁₄)-heteroaryloxy, N((C₁-C₁₄)-alkyl)₂, N((C₄-C₁₄)-aryl)₂, N((C₁-C₁₄)-alkyl)((C₄-C₁₄)-aryl), where alkyl, aryl, cycloalkyl, heteroalkyl, heteroaryl and heterocycloalkyl are each as defined above.

In one embodiment, R¹, R², R¹¹, R¹², R²¹, R²², R³², R³³, R⁴³, R⁴⁴ are selected from -H and/or a protecting group for amino functions described in "Greene's Protective Groups in Organic Synthesis" by P.G.M. Wuts and T.W. Greene, 4th edition, Wiley Interscience, 2007, p. 696-926.

In one embodiment, R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²³, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, R³⁰, R³¹, R³⁴, R³⁵, R³⁶, R³⁷, R⁴⁰, R⁴¹, R⁴², R⁴⁵, R⁴⁶, R⁴⁷, R⁴⁸, R⁴⁹, R⁵⁰ are selected from the group of hydrogen, hydroxyl, (C₁-C₁₂)-alkyl, (C₁-C₁₂)-heteroalkyl, (C₄-C₁₄)-aryl, (C₄-C₁₄)-aryl-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-heteroalkyl, O-(C₄-C₁₄)-aryl, O-(C₄-C₁₄)-aryl-(C₁-C₁₄)-alkyl, O-(C₃-C₁₄)-heteroaryl, O-(C₃-C₁₄)-heteroaryl-(C₁-C₁₄)-alkyl, O-(C₃-C₁₂)-cycloalkyl, O-(C₃-C₁₂)-cycloalkyl-(C₁-C₁₂)-alkyl, O-(C₃-C₁₂)-heterocycloalkyl, O-(C₃-C₁₂)-heterocycloalkyl-(C₁-C₁₂)-alkyl, S-(C₁-C₁₂)-alkyl, S-(C₄-C₁₄)-aryl, halogens, where the alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl groups mentioned are optionally mono- or polysubstituted.

In one embodiment, R¹, R², R¹¹, R¹², R²¹, R²², R³², R³³, R⁴³, R⁴⁴ are selected from: -H, (C₁-C₁₂)-acyl.

In one embodiment, R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²³, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, R³⁰, R³¹, R³⁴, R³⁵, R³⁶, R³⁷, R⁴⁰, R⁴¹, R⁴², R⁴⁵, R⁴⁶, R⁴⁷, R⁴⁸, R⁴⁹, R⁵⁰ are selected from: hydrogen, hydroxyl, (C₁-C₁₂)-alkyl, (C₄-C₁₄)-aryl, O-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-heteroalkyl, O-(C₄-C₁₄)-aryl, O-(C₃-C₁₂)-cycloalkyl, S-(C₁-C₁₂)-alkyl, S-(C₄-C₁₄)-aryl, halogens,
5 where the alkyl, heteroalkyl, cycloalkyl and aryl groups mentioned are optionally mono- or polysubstituted.

The process can be conducted at different carbon electrodes (glassy carbon, boron-doped diamond, graphite, carbon fibres, nanotubes, inter alia), metal oxide electrodes and metal
10 electrodes. Current densities in the range of 1-50 mA/cm² are applied.

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

The electrolysis is conducted in the customary electrolysis cells known to those skilled in the art. Suitable electrolysis cells are known to those skilled in the art.

20 One aspect of the invention is that the yield of the reaction can be controlled via the difference in the oxidation potentials (ΔE) of the two substrates.

The process according to the invention solves the problem mentioned at the outset.

25 For an efficient reaction regime, two reaction conditions are necessary:

- the substrate having the higher oxidation potential has to be added in excess, and
- the difference in the two oxidation potentials (ΔE) has to be within a particular range.

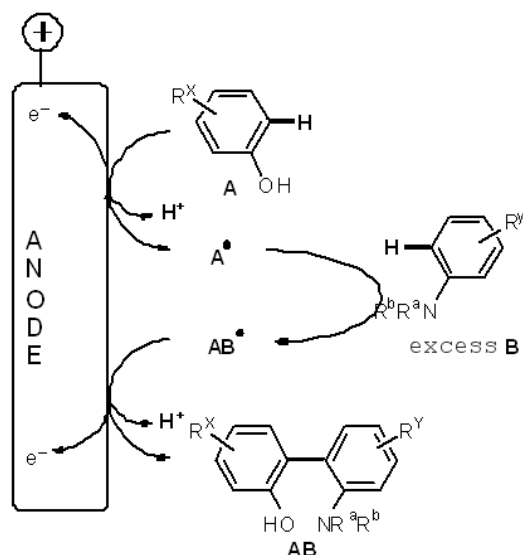
For the process according to the invention, the knowledge of the absolute oxidation potentials of
30 the phenols and anilines is not absolutely necessary. It is sufficient when the difference between the two oxidation potentials is known.

A further aspect of the invention is that the difference in the two oxidation potentials (ΔE) can be influenced via the solvents or solvent mixtures used.

For instance, the difference in the two oxidation potentials (ΔE) can be shifted into the desired range by suitable selection of the solvent/solvent mixture.

- 5 Proceeding from 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) as the base solvent, an excessively small ΔE can be increased, for example, by addition of alcohol. An excessively large ΔE , in contrast, can be lowered by addition of water.

The reaction sequence which proceeds is shown in the following scheme:



In the solvents mentioned, the selective oxidation of a phenol component **A** is enabled, this being able to be attacked nucleophilically by component **B** as a result of the high reactivity of the radical species formed. The first oxidation potentials of the two substrates appear to be crucial here for the success of the reaction. The controlled addition of protic additives such as MeOH or water to the electrolyte can enable a shift in precisely these oxidation potentials. Thus, it is possible to control yield and selectivity of this reaction.

With the aid of the process according to the invention, it has been possible for the first time to electrochemically prepare biaryls having hydroxyl and amino functions, and to dispense with multistage syntheses using metallic reagents.

If the aniline has the higher oxidation potential, in one variant of the process, the aniline is used in at least twice the amount relative to the phenol.

If the aniline has the higher oxidation potential, in one variant of the process, the ratio of phenol to aniline is in the range from 1:2 to 1:4.

If the phenol has the higher oxidation potential, in one variant of the process, the phenol is used in at least twice the amount relative to the aniline.

If the phenol has the higher oxidation potential, in one variant of the process, the ratio of aniline to phenol is in the range from 1:2 to 1:4.

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

In one variant of the process, the counterions of the conductive salts are selected from the 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.

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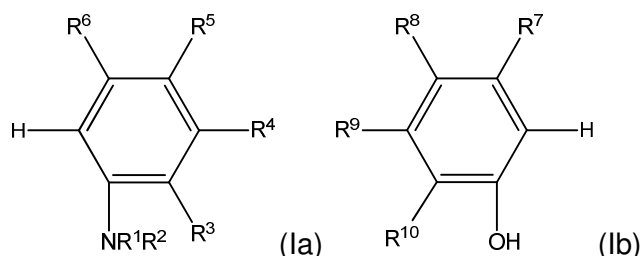
In one variant of the process, the reaction solution is free of fluorinated compounds.

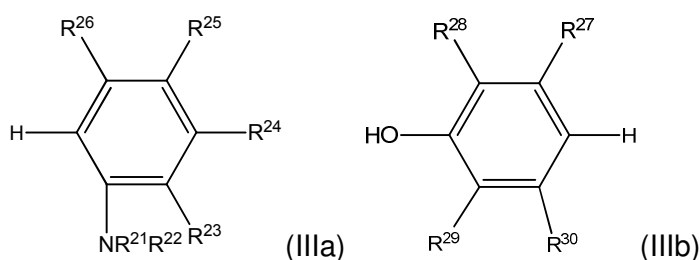
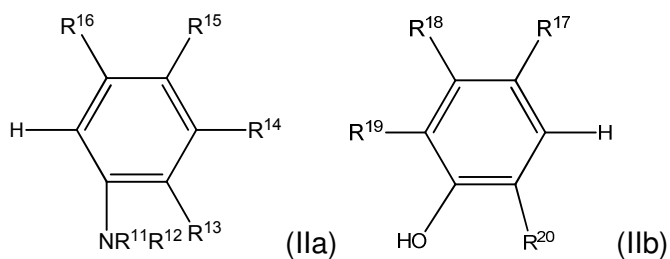
In one variant of the process, the reaction solution is free of transition metals.

In one variant of the process, the reaction solution is free of organic oxidizing agents.

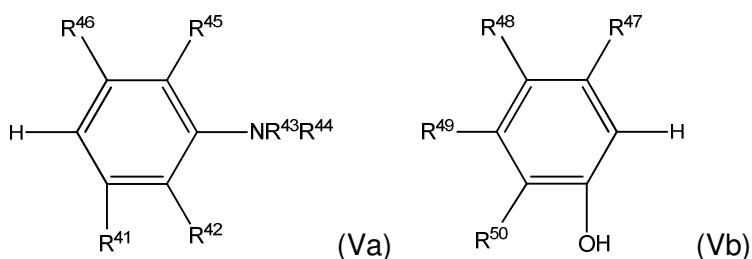
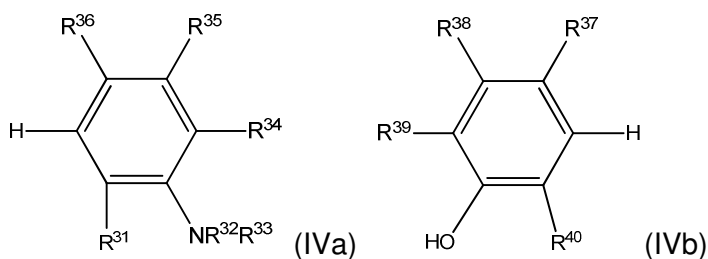
In one variant of the process, the phenol and the aniline are selected from: **Ia, Ib, IIa, IIb, IIIa, IIIb, IVa, IVb, Va, Vb**:

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where the substituents R¹ to R⁵⁰ are each independently selected from the group of hydrogen, hydroxyl, (C₁-C₁₂)-alkyl, (C₁-C₁₂)-heteroalkyl, (C₄-C₁₄)-aryl, (C₄-C₁₄)-aryl-(C₁-C₁₂)-alkyl, (C₄-C₁₄)-aryl-O-(C₁-C₁₂)-alkyl, (C₃-C₁₄)-heteroaryl, (C₃-C₁₄)-heteroaryl-(C₁-C₁₂)-alkyl, (C₃-C₁₂)-cycloalkyl, (C₃-C₁₂)-cycloalkyl-(C₁-C₁₂)-alkyl, (C₃-C₁₂)-heterocycloalkyl, (C₃-C₁₂)-heterocycloalkyl-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-heteroalkyl, O-(C₄-C₁₄)-aryl, O-(C₄-C₁₄)-aryl-(C₁-C₁₄)-alkyl, O-(C₃-C₁₄)-heteroaryl, O-(C₃-C₁₄)-heteroaryl-(C₁-C₁₄)-alkyl, O-(C₃-C₁₂)-cycloalkyl, O-(C₃-C₁₂)-

cycloalkyl-(C₁-C₁₂)-alkyl, O-(C₃-C₁₂)-heterocycloalkyl, O-(C₃-C₁₂)-heterocycloalkyl-(C₁-C₁₂)-alkyl, halogens, S-(C₁-C₁₂)-alkyl, S-(C₁-C₁₂)-heteroalkyl, S-(C₄-C₁₄)-aryl, S-(C₄-C₁₄)-aryl-(C₁-C₁₄)-alkyl, S-(C₃-C₁₄)-heteroaryl, S-(C₃-C₁₄)-heteroaryl-(C₁-C₁₄)-alkyl, S-(C₃-C₁₂)-cycloalkyl, S-(C₃-C₁₂)-cycloalkyl-(C₁-C₁₂)-alkyl, S-(C₃-C₁₂)-heterocycloalkyl, (C₁-C₁₂)-acyl, (C₄-C₁₄)-aroyl, (C₄-C₁₄)-aroyl-(C₁-C₁₄)-alkyl, (C₃-C₁₄)-heteroaroyl, (C₁-C₁₄)-dialkylphosphoryl, (C₄-C₁₄)-diarylphosphoryl, (C₃-C₁₂)-alkylsulphonyl, (C₃-C₁₂)-cycloalkylsulphonyl, (C₄-C₁₂)-arylsulphonyl, (C₁-C₁₂)-alkyl-(C₄-C₁₂)-arylsulphonyl, (C₃-C₁₂)-heteroarylsulphonyl, (C=O)O-(C₁-C₁₂)-alkyl, (C=O)O-(C₁-C₁₂)-heteroalkyl, (C=O)O-(C₄-C₁₄)-aryl,

where the alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl groups mentioned are optionally mono- or polysubstituted.

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Aryl for aromatic (hydrocarbyl) radicals, preferably having up to 14 carbon atoms, for example phenyl (C₆H₅-), naphthyl (C₁₀H₇-), anthryl (C₁₄H₉-), preferably phenyl.

Cycloalkyl for saturated cyclic hydrocarbons containing exclusively carbon atoms in the ring.

Heteroalkyl for an unbranched or branched aliphatic radical which may contain one to four, preferably one or two, heteroatom(s) selected from the group consisting of N, O, S and substituted N.

Heteroaryl for an aryl radical in which one to four, preferably one or two, carbon atom(s) may be replaced by heteroatoms selected from the group consisting of N, O, S and substituted N, where the heteroaryl radical may also be part of a larger fused ring structure.

Heterocycloalkyl for saturated cyclic hydrocarbons which may contain one to four, preferably one or two, heteroatom(s) selected from the group consisting of N, O, S and substituted N.

A heteroaryl radical which may be part of a fused ring structure is preferably understood to mean systems in which fused five- or six-membered rings are formed, for example benzofuran, isobenzofuran, indole, isoindole, benzothiophene, benzo(c)thiophene, benzimidazole, purine, indazole, benzoxazole, quinoline, isoquinoline, quinoxaline, quinazoline, cinnoline, acridine.

The substituted N mentioned may be monosubstituted, and the alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl groups may be mono- or polysubstituted, more preferably mono-, di- or trisubstituted, by radicals selected from the group consisting of hydrogen, (C₁-C₁₄)-alkyl, (C₁-C₁₄)-heteroalkyl, (C₄-C₁₄)-aryl, (C₄-C₁₄)-aryl-(C₁-C₁₄)-alkyl, (C₃-C₁₄)-heteroaryl, (C₃-C₁₄)-heteroaryl-(C₁-C₁₄)-alkyl, (C₃-C₁₂)-cycloalkyl, (C₃-C₁₂)-cycloalkyl-(C₁-C₁₄)-alkyl, (C₃-C₁₂)-heterocycloalkyl, (C₃-C₁₂)-heterocycloalkyl-(C₁-C₁₄)-alkyl, CF₃, halogen (fluorine, chlorine, bromine, iodine), (C₁-C₁₀)-haloalkyl, hydroxyl, (C₁-C₁₄)-alkoxy, (C₄-C₁₄)-aryloxy, O-(C₁-C₁₄)-alkyl-(C₄-C₁₄)-aryl, (C₃-C₁₄)-heteroaryloxy, N((C₁-C₁₄)-alkyl)₂, N((C₄-C₁₄)-aryl)₂, N((C₁-C₁₄)-alkyl)((C₄-C₁₄)-aryl), where alkyl, aryl, cycloalkyl, heteroalkyl, heteroaryl and heterocycloalkyl are each as defined above.

In one embodiment, R¹, R², R¹¹, R¹², R²¹, R²², R³², R³³, R⁴³, R⁴⁴ are selected from -H and/or a protecting group for amino functions described in "Greene's Protective Groups in Organic Synthesis" by P.G.M. Wuts and T.W. Greene, 4th edition, Wiley Interscience, 2007, p. 696-926.

In one embodiment, R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²³, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, R³⁰, R³¹, R³⁴, R³⁵, R³⁶, R³⁷, R⁴⁰, R⁴¹, R⁴², R⁴⁵, R⁴⁶, R⁴⁷, R⁴⁸, R⁴⁹, R⁵⁰ are selected from the group of hydrogen, hydroxyl, (C₁-C₁₂)-alkyl, (C₁-C₁₂)-heteroalkyl, (C₄-C₁₄)-aryl, (C₄-C₁₄)-aryl-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-heteroalkyl, O-(C₄-C₁₄)-aryl, O-(C₄-C₁₄)-aryl-(C₁-C₁₄)-alkyl, O-(C₃-C₁₄)-heteroaryl, O-(C₃-C₁₄)-heteroaryl-(C₁-C₁₄)-alkyl, O-(C₃-C₁₂)-cycloalkyl, O-(C₃-C₁₂)-cycloalkyl-(C₁-C₁₂)-alkyl, O-(C₃-C₁₂)-heterocycloalkyl, O-(C₃-C₁₂)-heterocycloalkyl-(C₁-C₁₂)-alkyl, S-(C₁-C₁₂)-alkyl, S-(C₄-C₁₄)-aryl, halogens, where the alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl groups mentioned are optionally mono- or polysubstituted.

In one embodiment, R¹, R², R¹¹, R¹², R²¹, R²², R³², R³³, R⁴³, R⁴⁴ are selected from: -H, (C₁-C₁₂)-acyl.

In one embodiment, R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²³, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, R³⁰, R³¹, R³⁴, R³⁵, R³⁶, R³⁷, R⁴⁰, R⁴¹, R⁴², R⁴⁵, R⁴⁶, R⁴⁷, R⁴⁸, R⁴⁹, R⁵⁰ are selected from the group of hydrogen, hydroxyl, (C₁-C₁₂)-alkyl, (C₄-C₁₄)-aryl, O-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-heteroalkyl, O-(C₄-C₁₄)-aryl, O-(C₃-C₁₂)-cycloalkyl, S-(C₁-C₁₂)-alkyl, S-(C₄-C₁₄)-aryl, halogens, where the alkyl, heteroalkyl, cycloalkyl and aryl groups mentioned are optionally mono- or polysubstituted.

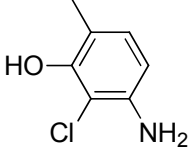
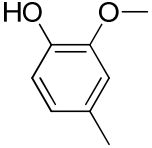
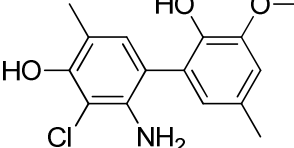
In this context, the following combinations are possible:

aniline	Ia	IIa	IIIa	IVa	Va
phenol	Ib	IIb	IIIb	IVb	Vb

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

5 Table 1:

Component 1	Component 2	Product	Yield (isolated) ^a	Selectivity (AB:BB) ^b
			33%	>100:1
			10%	>100:1
			14%	3:1
			18%	>100:1

			21%	30:1
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Electrolysis parameters: $n(\text{component 1}) = 5 \text{ mmol}$, $n(\text{component 1}) = 15 \text{ mmol}$, conductive salt:

MTBS, $c(\text{MTBS}) = 0.09 \text{ M}$, $V(\text{solvent}) = 33 \text{ ml}$, solvent: HFIP

Electrode material: glassy carbon, $j = 2.8 \text{ mA/cm}^2$, $T = 50^\circ\text{C}$, $Q = 2 F \cdot n(\text{component 1})$.

5 The electrolysis is effected under galvanostatic conditions.

^a: isolated yield based on $n(\text{component 1})$;

^b: determined via GC. AB: cross-coupling product, BB: homo-coupling product.

General procedures

10

Cyclic voltammetry (CV)

A Metrohm 663 VA stand equipped with a μ Autolab type III potentiostat was used (Metrohm AG, Herisau, Switzerland). *WE*: glassy carbon electrode, diameter 2 mm; *AE*: glassy carbon rod; *RE*: Ag/AgCl in saturated LiCl/EtOH. Solvent: HFIP + 0-25%v/v MeOH. Oxidation criterion: $j =$

15 0.1 mA/cm^2 , $\nu = 50 \text{ mV/s}$, $T = 20^\circ\text{C}$. Mixing during the measurement. $c(\text{aniline derivative}) = 151 \text{ mM}$, conductive salt: $\text{Et}_3\text{NMe O}_3\text{SOMe}$ (MTES), $c(\text{MTES}) = 0.09\text{M}$.

Chromatography

The preparative liquid chromatography separations via flash chromatography were conducted
20 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 beforehand by distillation on a rotary evaporator.

25 For thin-layer 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. Staining of the TLC plates was effected using a cerium-molybdatophosphoric acid solution as a dipping 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
30 sulphuric acid to 200 millilitres of water.

Gas chromatography (GC/GCMS)

The gas chromatography analyses (GC) of product mixtures and pure substances were effected with the aid of the GC-2010 gas chromatograph from *Shimadzu*, Japan. Measurement 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 µm; carrier gas: hydrogen; injector temperature: 250°C; detector temperature: 310°C; programme: “hard” method: start temperature 50°C for 1 min, heating rate: 15°C/min, final temperature 290°C for 8 min). Gas chromatography mass spectra (GCMS) of product mixtures and pure substances were recorded with the aid of the GC-2010 gas chromatograph combined with the GCMS-QP2010 mass detector from *Shimadzu*, Japan. Measurement 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 µm; carrier gas: hydrogen; injector temperature: 250°C; detector temperature: 310°C; programme: “hard” method: start temperature 50°C for 1 min, heating rate: 15°C/min, final temperature 290°C for 8 min; GCMS: ion source temperature: 200°C).

Melting points

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

Elemental analysis

The elemental analyses were conducted in the Analytical Division of the Department of Organic Chemistry at the Johannes Gutenberg University of Mainz on a Vario EL Cube from *Foss-Heraeus*, Hanau.

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 measured on an instrument of the MAT 95 XL sector-field instrument type from *Thermo Finnigan*, Bremen.

NMR Spectroscopy

The NMR spectroscopy studies were conducted on multi-nuclear 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 according to 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 with the number of bonds covered in Hertz (Hz). The numbers reported in the signal assignment correspond to the numbering given in the formula schemes, which need not correspond to IUPAC nomenclature.

GM1: General method for electrochemical cross-coupling

2-4 mmol of the respective deficiency component are dissolved together with 6-12 mmol of the respective second component to be coupled in the amounts of 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) and MeOH specified and converted in an undivided beaker cell with glassy carbon electrodes. The electrolysis is effected under galvanostatic conditions. The reaction is stirred and heated to 50°C with the aid of a water bath. After the end of the electrolysis, the cell contents are transferred together with HFIP into a 50 ml round-bottom flask and the solvent is removed under reduced pressure on a rotary evaporator at 50°C, 200-70 mbar. Unconverted reactant is retained by means of short-path distillation or Kugelrohr distillation (100°C, 10⁻³ mbar).

Electrode material

Anode: glassy carbon
Cathode: glassy carbon

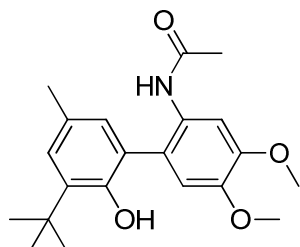
Electrolysis conditions:

Temperature [T]:	50°C
Current [I]:	25 mA
Current density [j]:	2.8 mA/cm ²
Quantity of charge [Q]:	2 F (per deficiency component)
Terminal voltage [U _{max}]:	3-5 V

Schematic cell structure

Figure 3 shows the structure of the cell in schematic form. This cell has the following components:

- 1“: stainless steel holders for electrodes
- 5 2“: Teflon stopper
- 3“: beaker cell with attached outlet for reflux condenser connection
- 4“: stainless steel clamp
- 5“: glassy carbon electrodes
- 6“: magnetic stirrer bar

N-Acetyl-2-amino-2'-hydroxy-4,5-dimethoxy-3'-(dimethylethyl)-5'-methylbiphenyl

The electrolysis is conducted according to GM1 in an undivided beaker cell with glassy carbon electrodes. To this end, 0.62 g (3.79 mmol, 1.0 equiv.) of 2-(dimethylethyl)-4-methylphenol and 2.22 g (11.36 mmol, 3.0 equiv.) of *N*-(3,4-dimethoxyphenyl)acetamide are dissolved in 25 ml of HFIP, 0.77 g of MTBS is added and the electrolyte is transferred to the electrolysis cell. After the electrolysis, the solvent and unconverted amounts of reactant are removed under reduced pressure, the crude product is purified by flash chromatography on silica gel 60 in a 4:1 eluent (CH:EA) and the product is obtained as a colourless solid.

Yield: 447 mg (33%, 1.3 mmol)

GC (*hard* method, HP-5): t_R = 16.14 min

R_f (CH:EA = 4:1) = 0.17

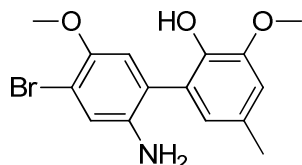
m_p = 182°C (recrystallized from DCM)

^1H NMR (400 MHz, CDCl_3) δ = 1.43 (s, 9H), 1.99 (s, 3H), 2.31 (s, 3H), 3.86 (s, 3H), 3.94 (s, 3H), 6.76 (s, 1H), 6.83 (d, J = 1.9 Hz, 1H), 6.94 (s, 1H), 7.14 (d, J = 1.9 Hz, 1H), 7.85 (s, 1H);

^{13}C NMR (101 MHz, CDCl_3) δ = 20.95, 24.49, 29.68, 35.01, 56.22, 56.28, 77.16, 106.54, 113.45, 118.74, 124.10, 128.32, 128.97, 129.48, 129.66, 136.89, 146.42, 149.37, 149.40, 168.91.

HRMS for $\text{C}_{21}\text{H}_{27}\text{NO}_4$ (ESI+) $[\text{M}+\text{H}]^+$: calc.: 358.2018, found: 358.2017

MS (EI, GCMS): m/z (%): 357 (100) $[\text{M}]^+$, 242 (100) $[\text{M}-\text{CH}_3]^+$, 315 (50) $[\text{M}-\text{C}_2\text{H}_2\text{O}]^+$.

2'-Amino-4'-bromo-2-hydroxy-3,5'-dimethoxy-5-methylbiphenyl

The electrolysis is conducted according to GM1 in an undivided beaker cell with glassy carbon electrodes. To this end, 0.43 g (2.15 mmol, 1.0 equiv.) of 4-bromo-3-methoxyaniline and 0.89 g (6.45 mmol, 3.0 equiv.) of 4-methylguaiacol are dissolved in 25 ml of HFIP, 0.77 g of MTBS is added and the electrolyte is transferred to the electrolysis cell. After the electrolysis, the solvent and unconverted amounts of reactant are removed under reduced pressure, the crude product is purified by flash chromatography on silica gel 60 in a 9:1 eluent (CH:EA) and the product is obtained as a brown oil.

Yield: 70 mg (10%, 0.2 mmol)

GC (*hard* method, HP-5): t_R = 16.82 min

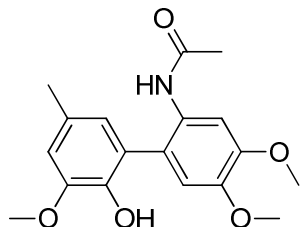
R_f (CH:EA = 4:1) = 0.26

1H NMR (400 MHz, DMSO- d_6) δ = 2.20 (s, 3H), 3.34 (bs, 3H), 3.75 (s, 3H), 3.77 (s, 3H), 6.48 (d, J = 1.9 Hz, 1H), 6.59 (s, 1H), 6.75 (d, J = 1.9 Hz, 1H), 7.06 (s, 1H);

^{13}C NMR (101 MHz, DMSO- d_6) δ = 20.68, 39.52, 55.81, 55.92, 98.31, 100.90, 111.86, 119.58, 120.97, 123.05, 124.50, 128.16, 134.14, 140.98, 143.99, 147.73, 154.88.

HRMS for $C_{15}H_{16}BrNO_3$ (ESI+) $[M+Na]^+$: calc.: 339.0392, found: 339.0390

MS (EI, GCMS): m/z (%): 339 (100) $[^{81}M]^+$, 337 (100) $[^{79}M]^+$, 320 (12) $[^{81}M-CH_3]^+$, 318 (12) $[^{79}M-CH_3]^+$.

N-Acetyl-2-amino-2'-hydroxy-5'-methyl-2',4,5-trimethoxybiphenyl

The electrolysis is conducted according to GM1 in an undivided beaker cell with glassy carbon electrodes. To this end, 0.52 g (3.79 mmol, 1.0 equiv.) of 4-methylguaiacol and 2.22 g (11.37 mmol, 3.0 equiv.) of *N*-(3,4-dimethoxyphenyl)acetamide are dissolved in 25 ml of HFIP, 0.77 g of MTBS is added and the electrolyte is transferred to the electrolysis cell. After the electrolysis, the solvent and unconverted amounts of reactant are removed under reduced

pressure, the crude product is purified by flash chromatography on silica gel 60 in a 2:3 eluent (CH:EA) + 1% AcOH and the product is obtained as a viscous, pale yellow oil.

Yield: 173 mg (14%, 0.52 mmol)

GC (*hard* method, HP-5): t_R = 16.11 min

5 R_f (CH:EA = 4:1) = 0.26

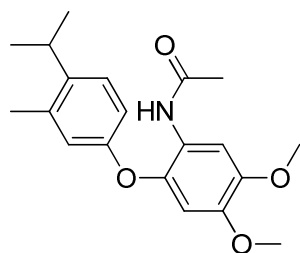
^1H NMR (400 MHz, CDCl_3) δ = 2.13 (s, 3H), 2.33 (s, 3H), 3.71 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 6.46 (s, 1H), 6.64-6.70 (m, 1H), 6.76 (d, J = 8.1 Hz, 1H), 6.79 (d, J = 1.9 Hz, 1H), 7.83 (bs, 1H), 8.07 (s, 1H);

10 ^{13}C NMR (101 MHz, CDCl_3) δ = 21.35, 24.80, 56.01, 56.35, 77.16, 103.27, 105.06, 113.51, 119.03, 121.55, 123.10, 134.57, 139.32, 143.77, 145.07, 145.14, 150.05, 168.34.

HRMS for $\text{C}_{18}\text{H}_{21}\text{NO}_5$ (ESI+) $[\text{M}+\text{Na}^+]$: calc.: 332.1498, found: 332.1499

MS (EI, GCMS): m/z (%): 331 (100) $[\text{M}]^+$, 289 (20) $[\text{M}-\text{C}_2\text{H}_2\text{O}]^+$, 318 (12) $[\text{M}-\text{C}_2\text{H}_5\text{NO}]^+$.

N-Acetyl-2-amino-3'-methyl-4'-(methylethyl)-4,5-dimethoxydiphenyl ether



15

The electrolysis is conducted according to GM1 in an undivided beaker cell with glassy carbon electrodes. To this end, 0.75 g (5.00 mmol, 1.0 equiv.) of 3-methyl-4-(methylethyl)phenol and 2.93 g (15.00 mmol, 3.0 equiv.) of *N*-(3,4-dimethoxyphenyl)acetamide are dissolved in 33 ml of HFIP, 1.02 g of MTBS are added and the electrolyte is transferred to the electrolysis cell. After the electrolysis, the solvent and unconverted amounts of reactant are removed under reduced pressure, the crude product is purified by flash chromatography on silica gel 60 in a 3:2 eluent (CH:EA) and the product is obtained as a colourless solid.

20

Yield: 313 mg (18%, 0.91 mmol)

GC (*hard* method, HP-5): t_R = 16.38 min

25 R_f (CH:EA = 3:2) = 0.26

m_p = 112°C (recrystallized from CH)

^1H NMR (400 MHz, CDCl_3) δ = 1.20 (s, 3H), 1.22 (s, 3H), 2.10 (s, 3H), 2.29 (s, 3H), 3.09 (hept, J = 6.9, 6.9, 6.8, 6.8, 6.8, 6.8 Hz, 1H), 3.74 (s, 3H), 3.90 (s, 3H), 6.52 (s, 1H), 6.65-6.79 (m, 2H), 7.16 (d, J = 8.4 Hz, 1H), 7.53 (s, 1H), 8.10 (s, 1H);

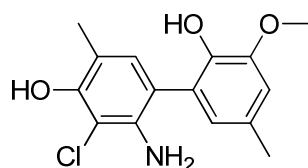
^{13}C NMR (101 MHz, CDCl_3) δ = 19.52, 23.43, 24.85, 28.84, 56.32, 56.35, 77.16, 104.23, 104.98, 114.49, 118.50, 123.77, 126.13, 137.07, 137.81, 141.81, 145.33, 145.44, 155.17, 168.31.

HRMS for $\text{C}_{20}\text{H}_{25}\text{NO}_4$ (ESI+) $[\text{M}+\text{Na}^+]$: calc.: 366.1681, found: 366.1676;

MS (EI, GCMS): $m/z(\%)$: 343 (100) $[\text{M}]^+$, 301 (20) $[\text{M}-\text{C}_2\text{H}_2\text{O}]^+$, 286 (80) $[\text{M}-\text{C}_2\text{H}_5\text{NO}]^+$.

5

2'-Amino-3'-chloro-2,4-dihydroxy-5,5'-dimethyl-3-methoxybiphenyl



The electrolysis is conducted according to GM1 in an undivided beaker cell with glassy carbon electrodes. To this end, 0.60 g (3.79 mmol, 1.0 equiv.) of 2-chloro-3-hydroxy-4-methylaniline and 1.57 g (11.36 mmol, 3.0 equiv.) of 4-methylguaiacol are dissolved in 25 ml of HFIP, 0.77 g of MTBS is added and the electrolyte is transferred to the electrolysis cell. After the electrolysis, the solvent and unconverted amounts of reactant are removed under reduced pressure, the crude product is purified by flash chromatography on silica gel 60 in a 4:1 eluent (CH:EA) and the product is obtained as a dark brown solid.

15 Yield: 221 mg (20%, 0.76 mmol)

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

R_f (CH:EA= 4:1)= 0.23

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ = 2.11 (s, 3H), 2.24 (s, 3H), 3.81 (s, 3H), 6.49 (s, 1H), 6.68 (s, 1H), 6.77 (s, 1H), 8.45 (bs, 1H), 8.77 (bs, 1H);

20 ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ = 16.12, 20.74, 55.83, 107.30, 111.57, 113.52, 116.93, 123.46, 126.07, 128.05, 130.42, 140.28, 141.07, 147.65, 150.18.

HRMS for $\text{C}_{15}\text{H}_{16}\text{ClNO}_3$ (ESI+) $[\text{M}+\text{H}^+]$: calc.: 294.0897, found: 294.0901

MS (EI, GCMS): $m/z(\%)$: 293 (100) $[\text{M}]^+$, 276 (100) $[\text{M}-\text{OH}]^+$.

25

Figure 1 shows a reaction apparatus in which the above-described coupling reaction can be conducted. The apparatus comprises a nickel cathode (1) and an anode of boron-doped diamond (BDD) on silicon or another support material, or another electrode material (5) known to those skilled in the art. The apparatus can be cooled with the aid of the cooling jacket (3). The arrows here indicate the flow direction of the cooling water. The reaction chamber is sealed with a Teflon stopper (2). The reaction mixture is mixed by a magnetic stirrer bar (7). On the anodic side, the apparatus is sealed by means of screw clamps (4) and seals (6).

30

Figure 2 shows a reaction apparatus in which the above-described coupling reaction can be conducted on a larger scale. The apparatus comprises two glass flanges (5'), through which, by means of screw clamps (2') and seals, electrodes (3') of boron-doped diamond (BDD)-coated support materials or other electrode materials known to those skilled in the art are pressed on. The reaction chamber can be provided with a reflux condenser via a glass sleeve (1'). The reaction mixture is mixed with the aid of a magnetic stirrer bar (4').

Figures 4 to 10 each show the change in the oxidation potential (V) as a function of the proportion of methanol (MeOH) to which the solvent 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) has been added. The numbers in the legends indicate the position of the substituent on the benzene ring in relation to the $-NH_2$ or the $-NH-CO-CH_3$ group: 2 = ortho, 3 = meta, 4 = para. It is clearly apparent from the figures that the oxidation potential can be altered by the addition of methanol.

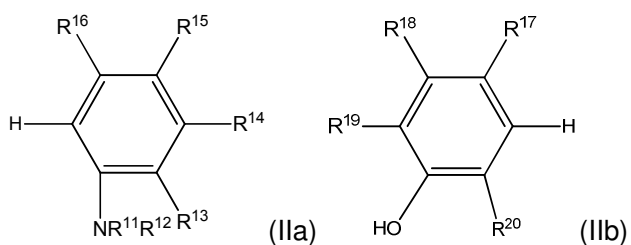
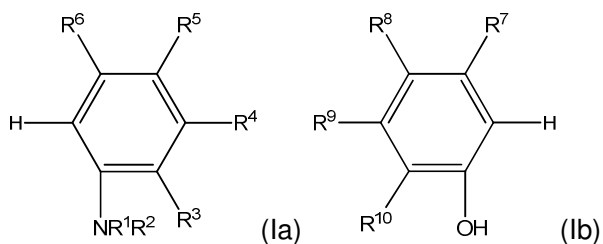
Claims

1. Electrochemical process for coupling phenol to aniline, comprising the process steps of:
 - 5 a") introducing a solvent or solvent mixture and a conductive salt into a reaction vessel,
 - b") adding an aniline having an oxidation potential E_{Ox1} to the reaction vessel,
 - c") adding a phenol having an oxidation potential E_{Ox2} to the reaction vessel, where:

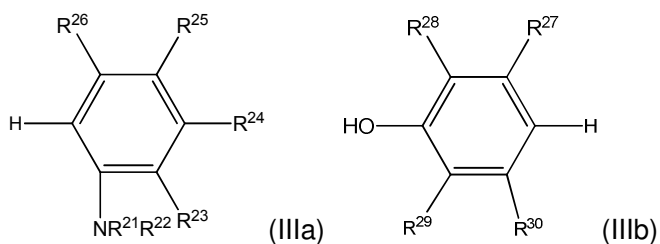
$$E_{Ox2} > E_{Ox1} \quad \text{and} \quad E_{Ox2} - E_{Ox1} = \Delta E,$$
 the phenol being added in excess relative to the aniline,
 - 10 and the solvent or solvent mixture being selected such that ΔE is within the range from 10 mV to 450 mV,
 - d") introducing two electrodes into the reaction solution,
 - e") applying a voltage to the electrodes,
 - f") coupling the phenol and the aniline.
- 15 2. Process according to Claim 1, wherein the phenol is used in at least twice the amount relative to the aniline.

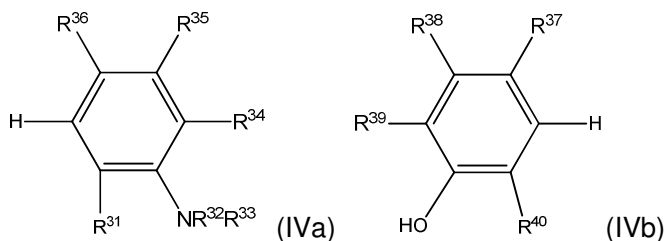
3. Process according to either of Claims 1 and 2,
wherein the ratio of aniline to phenol is in the range from 1:2 to 1:4.
- 5 4. Process according to any of Claims 1 to 3,
wherein the solvent or solvent mixture is selected such that ΔE is in the range from 20 mV to 400 mV.
5. Process according to any of Claims 1 to 4,
- 10 wherein the reaction solution is free of organic oxidizing agents.
6. Process according to any of Claims 1 to 5,
wherein the phenol and the aniline are selected from: **la**, **lb**, **Ila**, **Ilb**, **IIla**, **IIlb**, **IVa**, **IVb**, **Va**, **Vb**:

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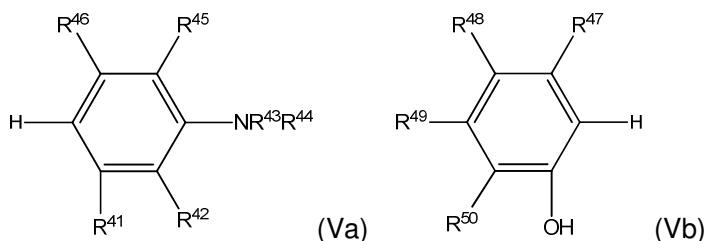


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5



where the substituents R^1 to R^{50} are each independently selected from the group of hydrogen, hydroxyl, (C₁-C₁₂)-alkyl, (C₁-C₁₂)-heteroalkyl, (C₄-C₁₄)-aryl, (C₄-C₁₄)-aryl-(C₁-C₁₂)-alkyl, (C₄-C₁₄)-aryl-O-(C₁-C₁₂)-alkyl, (C₃-C₁₄)-heteroaryl, (C₃-C₁₄)-heteroaryl-(C₁-C₁₂)-alkyl, (C₃-C₁₂)-cycloalkyl, (C₃-C₁₂)-cycloalkyl-(C₁-C₁₂)-alkyl, (C₃-C₁₂)-heterocycloalkyl, (C₃-C₁₂)-heterocycloalkyl-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-alkyl, O-(C₁-C₁₂)-heteroalkyl, O-(C₄-C₁₄)-aryl, O-(C₄-C₁₄)-aryl-(C₁-C₁₄)-alkyl, O-(C₃-C₁₄)-heteroaryl, O-(C₃-C₁₄)-heteroaryl-(C₁-C₁₄)-alkyl, O-(C₃-C₁₂)-cycloalkyl, O-(C₃-C₁₂)-cycloalkyl-(C₁-C₁₂)-alkyl, O-(C₃-C₁₂)-heterocycloalkyl, O-(C₃-C₁₂)-heterocycloalkyl-(C₁-C₁₂)-alkyl, halogens, S-(C₁-C₁₂)-alkyl, S-(C₁-C₁₂)-heteroalkyl, S-(C₄-C₁₄)-aryl, S-(C₄-C₁₄)-aryl-(C₁-C₁₄)-alkyl, S-(C₃-C₁₄)-heteroaryl, S-(C₃-C₁₄)-heteroaryl-(C₁-C₁₄)-alkyl, S-(C₃-C₁₂)-cycloalkyl, S-(C₃-C₁₂)-cycloalkyl-(C₁-C₁₂)-alkyl, S-(C₃-C₁₂)-heterocycloalkyl, (C₁-C₁₂)-acyl, (C₄-C₁₄)-aroyl, (C₄-C₁₄)-aroyl-(C₁-C₁₄)-alkyl, (C₃-C₁₄)-heteroaroyl, (C₁-C₁₄)-dialkylphosphoryl, (C₄-C₁₄)-diarylphosphoryl, (C₃-C₁₂)-alkylsulphonyl, (C₃-C₁₂)-cycloalkylsulphonyl, (C₄-C₁₂)-arylsulphonyl, (C₁-C₁₂)-alkyl-(C₄-C₁₂)-arylsulphonyl, (C₃-C₁₂)-heteroarylsulphonyl, (C=O)O-(C₁-C₁₂)-alkyl, (C=O)O-(C₁-C₁₂)-heteroalkyl, (C=O)O-(C₄-C₁₄)-aryl,

where the alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl groups mentioned are optionally mono- or polysubstituted, and

the following combinations are possible here:

aniline	Ia	IIa	IIIa	IVa	Va
phenol	Ib	IIb	IIIb	IVb	Vb