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Synthesis of Carbo[6]Helicene Derivatives Grafted with Amino or Aminoester Substituents from Enantiopure [6]Helicenyl Boronates

Nora Hellou,[†] Aurélie Macé,[†] Clothilde Martin,[†] Vincent Dorcet,[†] Thierry Roisnel,[†] Marion Jean,[‡] Nicolas Vanthuyne,[‡] Fabienne Berrée,[†] Bertrand Carboni,*[,†] Jeanne Crassous,*[,†]

[†] *Université de Rennes 1, Institut des Sciences Chimiques de Rennes, UMR CNRS 6226 Campus de Beaulieu, 35042, Rennes Cedex, France.* [‡] *Aix Marseille Univ, CNRS, Centrale Marseille, iSm2, Marseille, France.*

E-mail: bertrand.carboni@univ-rennes1.fr; jeanne.crassous@univ-rennes1.fr

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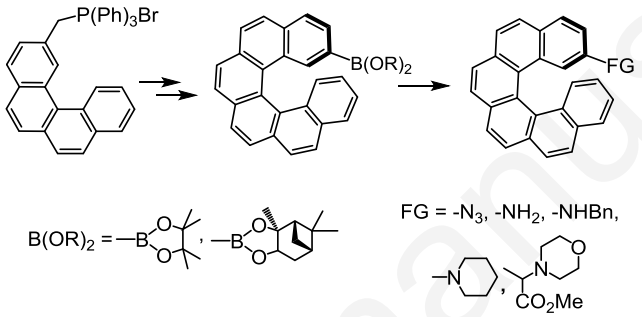

ABSTRACT. Enantiopure carbo[6]helicenyl boronates were synthesized using a photocyclisation reaction as the key step. These compounds were further converted to various amino derivatives using copper-catalyzed azidation or amination and reductive alkylation of benzylazide by a helicenyl dichloroborane. Asymmetric Petasis condensation with glyoxylic acid and morpholine controlled by the helical chirality afforded the corresponding amino esters.

[n]Helicenes are composed of n *ortho*-fused aromatic or heteroaromatic rings that display inherent helical chirality. Indeed, when n≥5, they become configurationally stable and can be obtained in enantiopure (*P*) and (*M*) forms by a diversity of methods.[1] Due to their unique screw shape and extended π-conjugation, helicenes display strong chiroptical properties (optical rotation values, circular dichroism and circularly polarized luminescence).[1] In the last decade, there has been a growing interest to use helicenes or analogues as building blocks for the design of chiral ligands for asymmetric catalysis,[2] materials for opto-electronics,[3] chiral sensors[4] or chiroptical switches.[5] In this context, the development of efficient strategies to tune the chiroptical properties of helicene-based derivatives by varying their structure remains of prime importance. Although a great number of organic helicenes have been synthesized,[1] simple amino derivatives still remain rather difficult to access. For example, only few helicenyl primary amines have been hitherto described in the literature (see **1**-**6**, Figure 1), although such compounds constitute key building blocks for further functionalization or for studying supramolecular assembly of π-helical systems.[6,7]

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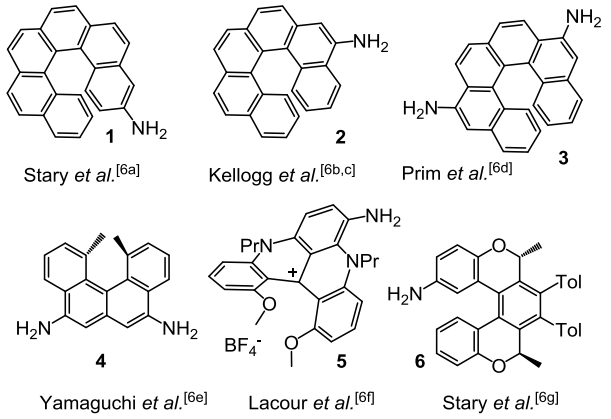
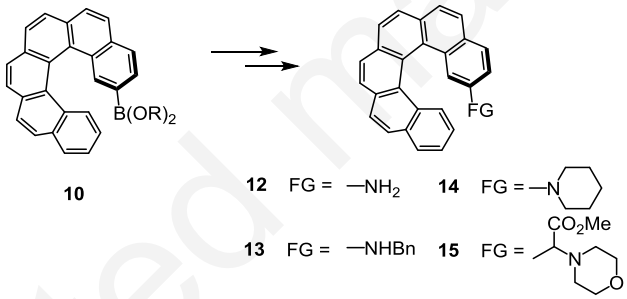


Figure 1. Helicenyl primary amines described in the literature.

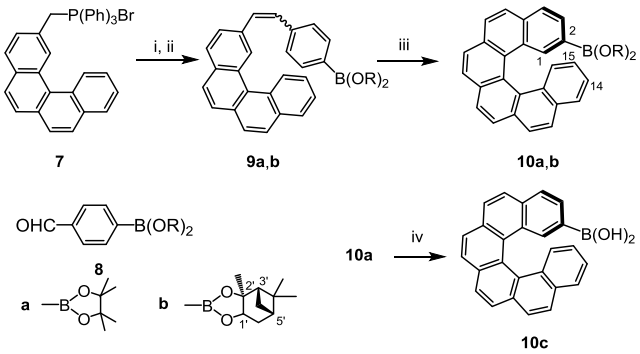
Most common methods introduce the amine functionality in a final stage *via*, for example, coupling of a bromohelicene,[6f,h] reduction of a nitro derivative,[6b] or Curtius rearrangement of a carboxylic acid.[6g] To our knowledge, none of them took advantage of the presence of boron, even though it can constitute a valuable source of a large variety of functional groups.[6c,6e,8,9]

In this manuscript, we report a straightforward access to enantiopure 2-carbo[6]helicene boronates **10** that are appealing precursors of the corresponding amino and aminoacid derivatives **12-15** (Schemes 1 and 2).



Scheme 1. Synthesis of (*M*)-amino- and aminoester substituted [6]helicenes **12**, **13**, **14** and **15**.

Racemic carbo[6]helicene (±)-**10a** bearing a pinacol boronic ester was first prepared in two steps (Scheme 2), *i.e.* by a Wittig reaction of 2-benzo[c]phenanthrylmethyl-phosphonium bromide **7** [10c] with pinacol 4-formyl-phenylboronate **8a** [11] (stereoselectivity *Z*/*E* = 80/20), followed by a photocyclization reaction using stoechiometric quantities of iodine and a large excess of propylene oxide, under high dilution conditions and using an immersion 150W Hg lamp. This approach enables to install the boronate moiety at the 2-position from the beginning of the synthesis, which proved its compatibility with the irradiation conditions.[12]



Scheme 2. Preparation of carbo[6]helicene-2-boronic pinacol ester (±)-**10a** and carbo[6]helicene-2-boronic pinanediol ester **10b**. Reagents and conditions: i) **8a** or **8b**, *n*-BuLi, THF, -78°C; ii) rt, 3 hrs, **9a**, 70% (*Z*/*E* = 80/20) and **9b** 89% (*Z*/*E* = 65/35); iii) *hν*, 1 eq. I_2, 40 eq. propylene oxide, toluene, 15 hrs, **10a**, 70% and **10b** 63%; iv) $NaIO_4$, NH_4OAc, acetone/water (2/1), rt, 4 d, 84% from (±)-**10a**.

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Helicenyl boronate (±)-**10a** was fully characterized by NMR and mass spectrometry. For instance, its ^{1}H NMR spectrum showed two signals at 1.21 and 1.22 ppm corresponding to the four diastereotopic methyl groups of the pinacol moiety and two doublets of doublet of doublet at 6.65 and 7.19 ppm for protons H-15 and H-14, respectively (see Supporting Information, SI). A characteristic signal was observed at 31.1 ppm in ^{11}B NMR. The conversion into the corresponding boronic acid **10c** was cleanly achieved in a 84 % yield by treatment with sodium periodate in an acetone/water mixture.[13] The pure (*P*)- and (*M*)- enantiomers of **10a** (with respective *ee*'s > 99.5%) were obtained by using HPLC separation over a chiral stationary phase (see SI). The chiroptical properties (electronic circular dichroism (ECD), specific and molar rotations (MR))[14] of (*P*)- and (*M*)-**10a** were then examined. The two mirror-image ECD spectra in CH_2Cl_2 solutions are depicted in Figure 2. They display the classical ECD signature for [6]helicene derivative, *i.e.* for (*P*)-**10a**, the strong negative band at 250 nm ($\Delta\varepsilon$ = -280 M^{-1} cm^{-1}) and a strong positive one at 330 nm ($\Delta\varepsilon$ = +307 M^{-1} cm^{-1}), with a clear vibronic structure. This ECD is comparable to carbo[6]helicenes.[10a,c] The specific and molar rotations[14] are high ((*P*)-(+)-**10a**: $[\alpha]_D^{23}$ = +2600, $[\phi]_D^{23}$ = +11800 (±7%), (*M*)-(-)-**10a**: $[\alpha]_D^{23}$ = -2800, $[\phi]_D^{23}$= -12700 (±7%, *C* 2 10^{-4} M, CH_2Cl_2) and again of similar magnitude compared to carbo[6]helicene ((*M*) enantiomer: $[\alpha]_D$ = -3860, $[\phi]_D$ = -11950 (*C* 10^{-3} M, $CHCl_3$).[10b]

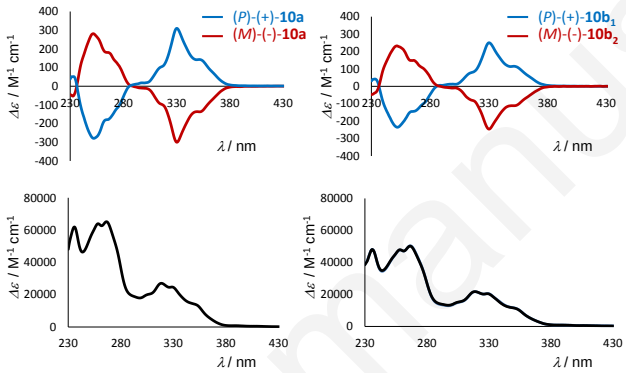


Figure 2. UV-vis and ECD spectra of enantiomers (*P*)-(+) and (*M*)-(-)-**10a** and of diastereomers (*P*,1'*S*,2'*S*,3'*R*,5'*S*)-**10b₁** and (*M*,1'*S*,2'*S*,3'*R*,5'*S*)-**10b₂** (*C* 5.10^{-5} M in CH_2Cl_2).

Similarly to **10a**, but using (1*S*,2*S*,3*R*,5*S*) pinanediol 4-formylphenylboronate **8b**[11] as starting aldehyde and following the same Wittig/photocyclization sequence as described above, was prepared the 2-carbo[6]helicenyl pinanediol boronate **10b**. Unfortunately, no asymmetric induction was observed in this process and a 1/1 diastereomeric mixture of (*P*,1'*S*,2'*S*,3'*R*,5'*S*) **10b₁** and (*M*,1'*S*,2'*S*,3'*R*,5'*S*) **10b₂** was obtained in a 63% overall yield. This lack of asymmetric induction could be due to the uncontrolled rotation around the carbon-boron bond which prevents the differentiation of both sides of the trigonal boron atom. The two pure diastereomers were isolated by HPLC (with respective *de*'s > 99.5%) and characterized by NMR and mass spectrometry. Their ^{1}H NMR spectra showed the typical signals for both the hexahelicene part and for the pinanyl moiety. As described in Figure 2, they display mirror-image relationship, since the pinanediol boronate unit has no ECD response in the UV-vis domain, and similar signature as for **10a** enantiomers, although with a lower intensity. Their specific and molar rotations are also almost mirror-image (for instance, (*P*)-(+)-**10b₁**: $[\alpha]_D^{23}$= +2370, $[\phi]_D^{23}$= +11990, (*M*)-(-)-**10b₂**: $[\alpha]_D^{23}$= -2640, $[\phi]_D^{23}$= -13360 (±7%, *C* 10^{-4} M, CH_2Cl_2)), again with low influence of the grafted pinanediol boronate.

Apart from column chromatographic separations,[1,15a,g] the few reported preparations of enantiopure helicene derivatives are essentially based on asymmetric catalysis,[15c,d] kinetic resolution,[15f] enantio-[15b] or diastereoselective syntheses.[9c,15e] Furthermore, although the parent carbo[n]helicenes have been known to form conglomerates,[16a] resolution of helicene enantiomers by crystallization methods has still been rarely used.[16] In the course of this work, we serendipitously observed that the two diastereomers **10b₁** and **10b₂** displayed very different solubilities in MeOH, with the pure diastereomer (*P*,1'*S*,2'*S*,3'*R*,5'*S*)-**10b₁** crystallizing out of the solution in 23% yield (a diastereomeric excess of ~23% in favour of (*M*,1'*S*,2'*S*,3'*R*,5'*S*)-**10b₂** was found for the solution).

Single crystals of (*M*)-**10a** and the less soluble diastereomer (*P*)-**10b₁** were then grown from a saturated solution in MeOH. The X-ray crystallography ascertained their structure and stereochemistry (see Figure 3).[17] For example, **10b₁** crystallized in the $P2_12_12_1$ space group, the helicene unit displaying a helicity (dihedral angle between the terminal rings) of 52.10°, which is typical for organic helicenes,[1] and the B-C bond showing a regular length of 1.56 Å.[8a] Note also that the boronate cycle deviates from coplanarity with the terminal phenyl ring by 20.02°. Finally, from view b in Figure 3, one can see that in the solid state the bulky part of the pinanediol unit is directed towards the helical core.

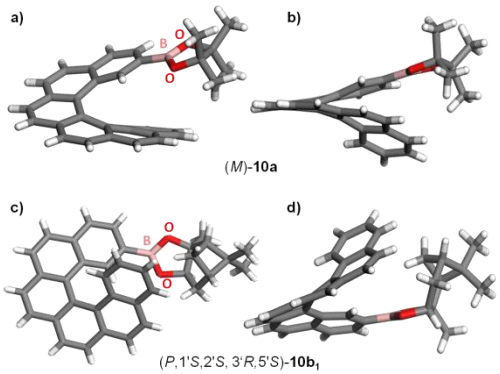
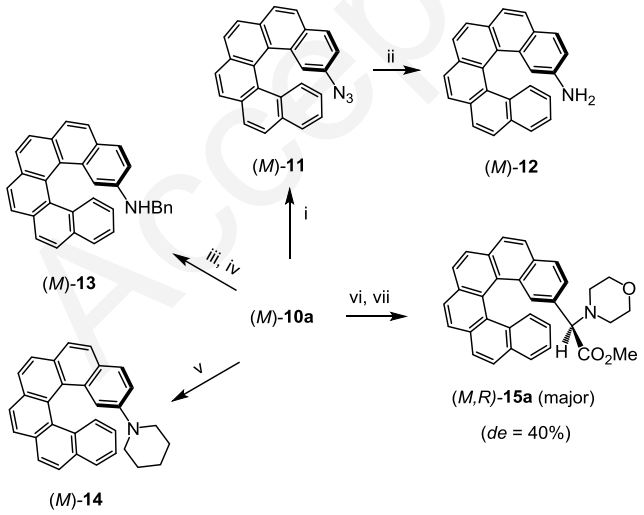


Figure 3. Two views of the X-ray crystallographic structures of (*M*)-**10a** (views **a** and **b**) and (*P*,1'*S*,2'*S*,3'*R*,5'*S*)-**10b₁** (views **c** and **d**)

Having the enantiopure boronates (*P*)- and (*M*)-**10a** in hands, we then turned our attention to their conversion to the corresponding amino and aminoacid derivatives **12-15** (Scheme 3). First attempts to directly introduce a NH_2 group from the boronic ester group by reaction with $H_2N\text{-}OSO_3H$[18] or $MeONH_2$[19] gave poor yields and irreproducible results that led us to envisage a two-step sequence. According to a reported procedure,[20] copper-catalyzed azidation of (*M*)-**10a** was carried out with copper sulfate in methanol at reflux for 19h. The resulting azide (*M*)-**11**, which could be isolated, but with a poor yield, was directly engaged in a hydrogenation step with H_2 in the presence of Pd/C to give (*M*)-**12** in an overall 75% yield. Note that the enantiomerically pure diastereomer (*P*,1'*S*,2'*S*,3'*R*,5'*S*)-**10b₁** was also successfully transformed to (*P*)-**12** using the same method, thus illustrating the possibility of straightforwardly preparing enantiopure 2-amino-helicene through a photocyclization-crystallization (*vide supra*)-amination, a process that can be particularly appealing for large-scale synthetic processes such as flow photochemistry.[10b]

The secondary *N*-benzyl helicenyl amine (*M*)-**13** was prepared from (*M*)-**10a** via conversion to the corresponding dichloroborane and then, without isolation of this sensitive intermediate, treatment with benzyl azide.[21] The formation of the piperidino derivative (*M*)-**14** was achieved in a moderate yield (44%) via a Chan-Lam amination using recently optimized reactions with copper acetate as catalyst and boric acid as additive.[22] The (*P*) enantiomers of **12** and **14** were also synthesized according to the same procedures. Finally, the transformation of (*M*)-**10a** to an amino ester derivative **15** was carried out via a three-component Petasis reaction with glyoxylic acid and morpholine, followed by esterification with (trimethylsilyl)diazomethane.[23] This condensation produced two diastereomeric compounds **15a**,**b** with a modest stereocontrol (*dr*: 7/3, measured by ^{1}H NMR of the crude mixture), which constitutes to our knowledge the first example of asymmetric induction controlled by the helicity of the aryl partner in this type of reaction. The structure of the minor isomer **15b** was ascertained by X-ray diffraction analysis (Figure 4).[17]



Scheme 3. Synthesis of (*M*)-helicenyl derivatives **12-15** from helicene-boronate (*M*)-**10a**. Reagents and conditions: i) NaN_3, $CuSO_4.5H_2O$, MeOH, reflux, 19h; ii) H_2 (1 atm), 10% Pd/C, EtOAc, rt, 21h, 75% (2 steps); iii) BCl_3, CH_2Cl_2, rt, 3h; iv) $PhCH_2N_3$, CH_2Cl_2, rt, 17h, 68% (two steps); v) $Cu(OAc)_2$, $B(OH)_3$, piperidine, MeCN, 80 °C, 26h, 44%; vi) morpholine, glyoxylic acid monohydrate, 1,1,1,3,3,3-hexafluoro-2-propanol, 60 °C, 48h; vii) (trimethylsilyl)diazomethane in diethyl ether, THF/MeOH, rt, 20h, 84% (two steps).

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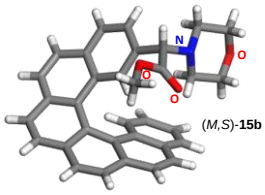

Figure 4. X-ray crystallographic structure of (*M, S*)-**15b** (minor isomer).

The UV-vis and ECD spectra of the new enantiopure compounds synthesized are depicted in Figure 5. It can be seen that the primary, secondary and tertiary amino-derivatives show very similar UV-vis and ECD spectra, with for example two absorption bands around 245 and 265 nm that are positively ECD-active ($\Delta\varepsilon \sim +115$ and $+75$ M^{-1} cm^{-1}) and two other ones around 325 and 350 nm that are negatively ECD-active ($\Delta\varepsilon \sim -100$ and -75 M^{-1} cm^{-1}) for the (*M*)-(-)-**12** and (*M*)-(-)-**14** enantiomers. As for the diastereomeric amino-ester grafted (*M*)-helicenes **15a** and **15b**, they display very similar UV-vis and ECD spectra that appeared much stronger than the amino-grafted ones, with a strong band around 250 nm ($\varepsilon > 50$ 10^3 M^{-1} cm^{-1}, $\Delta\varepsilon \sim +245$ to $+275$ M^{-1} cm^{-1}) and several strong ones between 300-400 nm ($\varepsilon > 20$ 10^3 M^{-1} cm^{-1}, $\Delta\varepsilon \sim -315$ to -77 M^{-1} cm^{-1}).

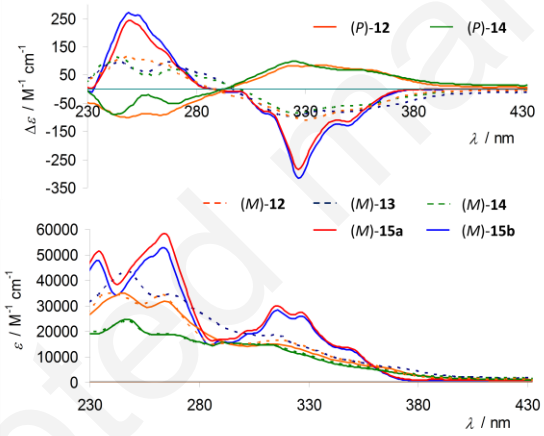

Figure 5. UV-vis and ECD spectra of enantiomers (*P*) and (*M*)-**12**, (*M*)-**13**, (*P*) and (*M*)-**14** and the two enantiopure diastereomers (*M*)-**15a** and (*M*)-**15b** (*C* ~ 5.10^{-5} M in CH_2Cl_2).

In summary, we have developed a straightforward set of reactions based on photocyclisation as key step that allow the efficient synthesis of enantiopure carbo[6]helicenyl boronates. These compounds are convenient precursors of several amino and aminoacid derivatives via chemical transformation of the boronic ester moiety. Compared to other multi-step processes described in the literature,[6] this strategy appears short and very simple. Application of this chemistry to other functionalized helicenes and development of these new organoboranes are in progress in our groups.

EXPERIMENTAL SECTION

Solvents were freshly distilled under argon from sodium / benzophenone (THF) or from phosphorus pentoxide (CH_2Cl_2 = DCM). All commercially available chemicals were used without further purification. Column chromatography purifications were performed over silica gel (Merck Geduran 60, 0.063–0.200 mm). Flash chromatography purifications were performed on a Grace Reveleris™ with Puriflash™ 15µm flash cartridges (Interchim). Irradiation reactions were conducted using a Heraeus TQ 150 mercury vapor lamp. NMR spectra were recorded at room temperature on a Bruker AV III 300 MHz spectrometer, a Bruker AV III 400 MHz equipped with a tunable BBFO probe, a Bruker Av III HD 500 MHz fitted with a tunable BBO probe (Biosit platform, Université de Rennes 1). ^{1}H and ^{13}C chemical shifts are reported in parts per million (ppm) relative to Me_4Si as external standard. Mass spectrometry was performed by the CRMPO, University of Rennes 1, on

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a LC-MS Agilent 6510 or a Thermo Fisher Q-Exactive using ESI technique. Melting points were measured on a melting point apparatus Stuart SMP10. Specific rotations (in deg cm^3g^{-1}) were measured in a 1 dm thermostated quartz cell on a Perkin Elmer-341 polarimeter. Circular dichroism (in $M^{-1}cm^{-1}$) was measured on a Jasco J-815 Circular Dichroism Spectrometer IFR140 facility (Biosit platform, Université de Rennes 1). UV/vis spectroscopy was conducted on a Varian Cary 5000 spectrometer. Chiral high-performance liquid chromatography (HPLC) was performed by iSm2, Aix Marseille University, on an Agilent Technologies 1260 Infinity with Igloo-Cil ovens, using Jasco OR-1590 and CD-2095 as polarimetric and circular dichroïsm detectors. The analytical (250x4.6 mm) and preparative (250x10 mm) columns used are (*S*,*S*)-Whelk-O1 from Regis Technologies (Morton Grove, USA), Chiralpak IA, and Chiralpak IB.

2-Benzo[c]phenanthrylmethylphosphonium bromide **7**,[10c] *p*-benzaldehyde pinacol boronate **8a** and *p*-benzaldehyde pinanediol boronate **8b** were prepared according to the literature.[11]

General procedure for 2-carbo[6]helicene pinacol and pinanediol boronates 10.

*Synthesis of 2-styrylbenzo[c]phenanthrenes (**9**).* A suspension of 2-benzo[c]phenanthrylmethylphosphonium bromide **7** (375 mg, 0.64 mmol, 1 eq.) in 18 mL of anhydrous THF, under argon, was cooled to -78 °C. To the stirred suspension was added dropwise *n*-BuLi (2.5 M in hexanes, 0.26 ml, 0.64 mmol, 1 eq.). The reaction mixture turned deep red and then slowly was warmed up to room temperature. Stirring was continued further for 45 min and, after cooling to -78 °C, was added dropwise a solution of the boronate **8a** or **8b** (0.61 mmol, 0.95 eq.) in 1 mL of THF. The reaction mixture was warmed up to room temperature and stirring was maintained for 3h, while the solution turns yellow. 10 mL of pentane were added and the reaction mixture was filtered over Celite® and concentrated under vacuum. The crude oily product was purified by column chromatography on silica gel.
Pinacol (4-(2-(benzo[c]phenanthren-2-yl)vinyl)phenyl) boronic ester (*Z*/*E*=80/20) ***(9a)***. 206 mg, 70%. Yellowish solid, mp = 62-64° C, R_f = 0.75 and 0.70 (cyclohexane/CH_2Cl_2, 2/8). (*Z*)-isomer, ^{1}H NMR (300 MHz, $CDCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.42 (d, *J* = 8.5 Hz, 1H), 7.98 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.95-7.27 (m, 12H), 6.95 (d, *J* = 12.1 Hz, 1H), 6.83 (d, *J* = 12.1 Hz, 1H), 1.37 (s, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5, 135.2, 133.5, 132.6, 131.8, 131.3, 130.9, 130.5, 130.3, 128.7, 128.6, 128.4, 127.7, 127.6, 127.3, 127.0, 126.9, 126.8, 126.4, 125.8, 83.9, 25.0. ^{11}B NMR (96 MHz, $CDCl_3$) δ 31.0. HRMS (ESI) $[M+Na]^+$calculated for $C_{32}H_{29}O_2BNa$ 479.2158, found 479.2151.
(1S',2S',3R',5S') Pinanediol (4-(2-(benzo[c]phenanthren-2-yl)vinyl)phenyl) boronic ester (*Z*/*E*=65/35) ***(9b)***. 290 mg, 89 %. Yellowish solid. R_f = 0.95 (CH_2Cl_2). (*Z*)-isomer, ^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.92 (s, 1H), 8.35 (d, J = 8.5 Hz, 1H), 8.03 (t, J = 8.3 Hz, 1H), 7.95-7.27 (m, 12H), 6.91 (d, J = 11.9 Hz, 1H), 6.79 (d, J = 12.2 Hz, 1H), 4.43 (dd, J = 8.8, 1.4 Hz, 1H), 1.46 (s, 3H), 1.30 (s, 3H), 1.18 (d, J = 10.7 Hz, 1H), 0.88 (s, 3H).

*Synthesis of helicenylboronate (**10**).* Boronate **9** (0.39 mmol, 1 eq.) (*Z*/*E* mixture), iodine (100 mg, 0.39 mmol, 1 eq.) and propylene oxide (1,1 mL, 15.6 mmol, 40 eq.) were dissolved in toluene (2.5 L) previously degazed, and placed in a photoreactor equipped with an immersion lamp (150W). The mixture was irradiated for 22 hours. After evaporation of the solvent, the residue was purified by column chromatography on silica gel. The two pure enantiomers or diastereomers were then separated by using HPLC.

(±) *Pinacol hexahelicen-2-ylboronic ester (**10a**)*. 125 mg, 70 %. Yellowish solid, mp = 238-240 °C. R_f = 0.10 (cyclohexane/CH_2Cl_2, 8/2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (s, 1H), 8.04-7.87 (m, 8H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.77 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.61 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.57 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.19 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 6.65 (ddd, *J* = 8.5, 6.9, 1.3 Hz, 1H), 1.22 (s, 6H), 1.21 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.1, 133.7, 133.2, 132.2, 131.5, 131.2, 130.3, 129.9, 129.0, 128.4, 128.3, 127.9, 127.8, 127.73, 127.72, 127.51, 127.48, 127.2, 127.0, 126.9, 126.6, 126.3, 125.4, 124.5, 124.3, 83.5, 25.1, 24.5 (the carbon α to boron was not found). ^{11}B NMR (96 MHz, $CDCl_3$) δ 31.1. HRMS (ESI) $[M+Na]^+$ calculated for $C_{32}H_{27}O_2BNa$ 477.2002, found 477.2002.

HPLC conditions: (*S*,*S*)-Whelk-O1, *n*-heptane/isopropanol/ dichloromethane 90/5/5, flow rate = 1.0 mL/min, UV 254 nm, t_R (*P*) = 6.98 min and t_R, (*M*) = 8.14 min. (*P*)-**10a**: mp = 214 °C. *ee* = 99.6%, $[\alpha]_D^{23}$ = +2600 (±7%, CH_2Cl_2, 2 10^{-4} mol.L^{-1}). (*M*)-**10a**: mp = 214 °C. *ee* = 99.4%, $[\alpha]_D^{23}$ = -2800 (±7%, CH_2Cl_2, 2 10^{-4} mol.L^{-1}).

(1'S,2'S,3'R,5'S)-Pinanediol hexahelicen-2-ylboronic ester (***10b***). 124 mg, 63%. Yellowish solid. HPLC conditions for **10b₁** and **10b₂**: Chiralpak IB, *n*-heptane/isopropanol 95/5, flow rate = 1.0 mL/min, UV 254 nm, t_R (**10b₁**) = 5.01 and t_R (**10b₂**) = 4.40 min.

10b₁ could be also directly obtained by crystallization according to the following procedure. 43 mg of a 1/1 diastereomeric mixture of **10b₁** and **10b₂** was heated at reflux in 1 mL of MeOH. After 10 mn, the mixture was cooled to room temperature and kept at this temperature for half an hour. 15 mg of pure **10b₁** (*de*>99.5%, measured by HPLC) was collected by filtration. Evaporation of the mother liquors afforded the diastereomerically enriched **10b₂** with a *de* of 23%.

(*P*)-**10b₁**: mp = 196-198° C. R_f = 0.33 (cyclohexane/CH_2Cl_2, 8/2). *de* = 99.5%, ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.09-7.99 (m, 7H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.90 (d, *J* = 9.0 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.74 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 6.63 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 4.19 (dd, *J* = 8.7, 2.0 Hz, 1H), 2.37-2.29 (m, 1H), 2.26-2.08 (m, 1H), 2.001.98 (m, 2H), 1.82 (dt, *J* = 14.3, 2.3 Hz, 1H), 1.34 (s, 3H), 1.32 (s, 3H), 1.02-0.88 (m, 1H), 0.85 (s, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 136.3, 134.1, 133.8, 132.7, 131.84, 131.79, 130.7, 130.3, 129.3, 128.7, 128.6, 128.41, 128.35, 128.2, 128.1, 127.9, 127.7, 127.5, 127.4, 127.2, 126.7, 125.9, 125.0, 124.5, 86.6, 78.5, 52.0, 40.1, 38.6, 35.7, 28.8, 27.4, 27.0, 24.3 (the carbon α to boron was not found). ^{11}B NMR (96 MHz, $CDCl_3$) δ 30.2. HRMS (ESI) $[M+Na]^+$ calculated for $C_{36}H_{31}O_2BNa$ 529.2309, found 529.2311. $[\alpha]_D^{23}$ = +2370, $[\phi]_D^{23}$ = +11990 (±7%, CH_2Cl_2, 10^{-4} mol.L^{-1}).

(*M*)-**10b₂**: mp = 88-90 °C. R_f = 0.36 (cyclohexane/CH_2Cl_2, 8/2). *de* = 99.5%, ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.07-7.90 (m, 9H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.79 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.55 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.51 (dd, *J* = 8.7, 1.1 Hz, 1H), 7.19 (ddd, *J* = 8.0, 6.9, 1.2 Hz, 1H), 6.63 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 4.24 (dd, *J* = 8.7, 2.0 Hz, 1H), 2.36-2.23 (m, 2H), 2.01 (t, *J* = 5.6 Hz, 1H), 1.94-1.88 (m, 1H), 1.76 (ddd, *J* = 14.5, 3.4, 2.0 Hz, 1H), 1.37 (s, 3H), 1.26 (s, 3H), 0.89 (d, *J* = 11.0 Hz, 1H), 0.85 (s, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 136.0, 134.1, 133.7, 132.8, 131.79, 131.77, 130.7, 130.2, 129.5, 128.7, 128.6, 128.44, 128.39, 128.2, 128.0, 127.9, 127.7, 127.44, 127.36, 127.2, 126.5, 125.7, 124.9, 124.5, 86.2, 78.7, 52.0, 40.2, 38.7, 35.9, 28.9, 27.5, 27.4, 24.3 (the carbon α to boron was not found). ^{11}B NMR (96 MHz, $CDCl_3$) δ 30.2. HRMS (ESI) $[M+Na]^+$ calculated for $C_{36}H_{31}O_2BNa$ 529.2309, found 529.2312. $[\alpha]_D^{23}$ = -2640, $[\phi]_D^{23}$ = -13360 (±7%, CH_2Cl_2, 10^{-4} mol.L^{-1}).

*(±)-Hexahelicen-2-ylboronic acid (**10c**).* To a solution of [6]helicenylboronate (±)-**10a** (30 mg, 0.066 mmol, 1 eq.) in a mixture of acetone (4 mL) and water (2 mL) were added sodium periodate (85 mg, 0.40 mmol, 6 eq.) and ammonium acetate (31 mg, 0.40 mmol, 6 eq.). The solution was vigorously stirred at r.t for 4 days. The solvent was removed under vacuum and the resulting crude material was diluted with diethyl ether and washed with water. The organic layer was then dried over $MgSO_4$ and concentrated under reduced pressure to give the boronic acid **10c** as a brownish solid (21 mg, 84 %). mp = 134-138 °C. R_f = 0.15 (cyclohexane/ AcOEt, 7/3). ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.21-7.95 (m, 9H), 7.86 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.61 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.39 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.39 (s, 2H), 7.19 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 6.60 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 134.1, 132.7, 132.4, 131.7, 130.9, 130.7, 130.5, 129.0, 128.5, 128.0, 127.8, 127.7 (2C), 127.5, 127.4, 127.2, 126.8 (2C), 126.7, 126.6, 126.1, 125.4, 124.3, 123.1 (the carbon α to boron was not found). ^{11}B NMR (96 MHz, $CDCl_3$) δ 30.4.

*(M)-2-Aminohexahelicene (**12**).* To a solution of NaN_3 (55 mg, 0.84 mmol, 2.6 eq.) and $CuSO_4.5H_2O$ (3 mg, 0.010 mmol, 0.23 eq.) in MeOH (1.5 mL) was added the boronate (*M*)-**10a** (20 mg, 0.044 mmol, 1 eq.). The solution was vigorously stirred at reflux for 19h. After evaporation of MeOH, EtOAc (2 mL) and 10% Pd/C (8 mg) were added. A balloon filled with dihydrogen gas under atmospheric pressure was adapted to the reaction vessel through a needle. The solution was first purged by three cycles of vacuum and dihydrogen, refilling, then flushed again with the dihydrogen. After stirring overnight, the solvent was removed under vacuum and the residue was subjected to chromatography (silica gel, cyclohexane/CH_2Cl_2, 7/3 as eluent) to afford the amino derivative (*M*)-**12**. (12 mg, 75 %). Yellowish solid, mp = 195-197 °C. R_f = 0.10 (cyclohexane/ CH_2Cl_2, 7/3).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-7.91 (m, 6H), 7.89-7.78 (m, 2H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.32 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 6.82 (d, *J* = 2.3 Hz, 1H), 6.79 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 6.67 (dd, *J* = 8.4, 2.3 Hz, 1H), 3.00 (br, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 133.0, 132.2, 131.7, 131.4, 131.3, 130.4, 129.0, 127.9, 127.8, 127.7, 127.6, 127.4, 127.3, 127.1, 126.93, 126.86, 126.8, 126.5, 126.0, 125.9, 124.7, 124.5, 122.8, 116.3, 111.8. HRMS (ESI) $[M+H]^+$ calculated for $C_{26}H_{18}N$ 344.1439, found 344.1434. $[\alpha]_D^{23}$ = -3210, $[\phi]_D^{23}$ = -11020 (±7%, CH_2Cl_2, 2.85 10^{-4} mol.L^{-1}).
Similarly, the (*P*)-**12** enantiomer could be prepared starting from enantiopure isomer *(P)*-**10a**. (*P*)-**12**: $[\alpha]_D^{23}$ = +2990, $[\phi]_D^{23}$ = +10270 (±7%, CH_2Cl_2, 3.0 10^{-4} mol.L^{-1}).

*(M)-2-(N-Benzylamino)hexahelicene (**13**).* In a Schlenk tube equipped with a septum under argon were introduced (*M*)-**10a** (20 mg, 0.044 mmol, 1 eq.) and CH_2Cl_2 (0.5 mL). Boron trichloride (1M solution in hexane, 0.22 mL, 0.22 mmol, 5 eq.) was then added at 0°C. After 3h at r.t, the solvent and the excess of BCl_3 were removed under vacuum and the residue was taken up with CH_2Cl_2 (0.5 mL) and benzyl azide (17µL, 0.13 mmol, 3 eq.) at 0°C. After 17h at r.t., AcOEt (10 mL) and 2N NaOH (0.5 mL) were successively added. The organic layer was separated, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by chromatography (silica gel, cyclohexane/CH_2Cl_2 : 6/4 as eluent) to give **13** as a yellow oil (13 mg, 68 %). R_f = 0.60 (cyclohexane/ CH_2Cl_2, 5/5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01-7.89 (m, 6H), 7.89 (dd,

J = 8.0, 1.3 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.77 (dd, *J* = 8.6, 1.0 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.34 (ddd, *J* = 7.9, 6.8, 1.2 Hz, 1H), 7.28-7.17 (m, 3H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.81 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 6.76 (d, *J* = 2.3 Hz, 1H), 6.63 (dd, *J* = 8.6, 2.3 Hz, 1H), 3.54 (br, 1H), 3.39 (d, *J* = 13.5 Hz, 1H), 3.34 (d, *J* = 13.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.7, 139.1, 133.1, 132.3, 131.7, 131.6, 131.3, 130.7, 128.8, 128.5 (2C), 127.93, 127.89, 127.8 (2C), 127.7, 127.5, 127.3, 127.2, 127.14, 127.10, 126.8 (2C), 125.9, 125.4, 124.8, 124.6, 122.3, 115.9, 107.9, 47.7. HRMS (ESI) $[M+Na]^+$ calculated for $C_{33}H_{23}NNa$ 456.1728, found 456.1725. $[\alpha]_D^{23}$ = -3260, $[\phi]_D^{23}$ = -14150 (±7%, CH_2Cl_2, 2.3 10^{-4} mol.L^{-1}).

*(M)-2-(Piperidin-1-yl)hexahelicene (**14**).* (*M*)-**10a** (20 mg, 0.044 mmol, 1 eq.), powdered activated 4 Å molecular sieves (15 mg), $Cu(OAc)_2$ (10 mg, 0.055 mmol, 1,25 eq.), $B(OH)_3$ (8 mg, 0.13 mmol, 2.94 eq.), and piperidine (9 µL, 0.088 mmol, 2.00 eq.) in MeCN (0,2 mL) were sealed in an Ace pressure tube under air and stirred at 80 °C (preheated sand bath, sand temperature) for 26 h. The reaction mixture was allowed to reach to room temperature, filtered through Celite. The filtrate was concentrated under vacuum and the residue was purified by flash chromatography (cyclohexane/CH_2Cl_2, 8/2 as eluent) to give **14** as a yellowish solid (8 mg, 44 %). mp = 44-48 °C. R_f = 0.30 (cyclohexane/CH_2Cl_2, 5/5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04-7.92 (m, 5H), 7.88 (d, *J* = 8.6 Hz, 1H), 7.85-7.80 (m, 2H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 4.0 Hz, 1H), 7.70 (d, *J* = 4.2 Hz, 1H), 7.26 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H), 7.05 (s, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.75 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 2.45-2.38 (m, 2H), 2.33-2.22 (m, 2H), 1.45-1.34 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.0, 133.2, 132.0, 131.3, 131.1, 130.3, 128.3, 128.0, 127.8, 127.7 (2C), 127.6 (2C), 127.4, 127.3, 127.1, 127.0, 126.8 (2C), 126.4, 126.0, 125.0, 124.4, 123.5, 119.1, 113.4, 50.7, 25.8, 24.2. HRMS (ESI) $[M+Na]^+$ calculated for $C_{31}H_{25}NNa$ 434.1885, found 434.1878. $[\alpha]_D^{23}$ = -2600, $[\phi]_D^{23}$ = -10360 (±7%, CH_2Cl_2, 2.0 10^{-4} mol.L^{-1}).

Similarly, the (*P*)-**14** enantiomer could be prepared starting from enantiopure isomer *(P)*-**10a**. (*P*)-**14**: $[\alpha]_D^{23}$ = +2430, $[\phi]_D^{23}$ = +9685 (±7%, CH_2Cl_2, 2.1 10^{-4} mol.L^{-1}).

(M,R)- and (M,S)-Methyl-2-(hexahelicen-2-yl)-2-morpholinoacetate **15**. (*M*)-**10a** (40 mg, 0.088 mmol, 1 eq.), morpholine (22 µL, 0.26 mmol, 3 eq.), and glyoxylic acid monohydrate (24 mg, 0.26 mmol, 3 eq.) in 1,1,1,3,3,3-hexafluoro-2-propanol (2 mL) were sealed in an Ace pressure tube under air and stirred at 60 °C for 48 h. The reaction mixture was allowed to cool down to room temperature, and concentrated under vacuum. THF (1 mL), MeOH (0,5 mL) and (trimethylsilyl)diazomethane solution (2M in diethyl ether) (0,13 mL, 0.26 mmol, 3 eq.) were then successively added. After 20 h at r.t and concentration under reduced pressure, the residue (7/3 mixture of two diastereomers) was purified by flash chromatography (cyclohexane/AcOEt : 9/1 as eluent) to give the two diastereomers (*M*)-**15** (42 mg, 84 %).
Major isomer (*M,R*)-**15a**: 29 mg, mp = 107-111 °C (decomp.). R_f = 0.30 (cyclohexane/AcOEt, 7/3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-7.94 (m, 7H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.87-7.83 (m, 2H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.59-7.55 (m, 2H), 7.16 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 6.69 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H), 3.80-3.58 (m, 4H), 3.35 (s, 3H), 3.05 (s, 1H), 1.99-1.75 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 133.4, 132.8, 132.3, 132.1, 131.6, 131.5, 130.2, 130.0, 129.7, 128.7, 128.14, 128.11, 128.0, 127.8, 127.7, 127.6, 127.3, 127.2, 127.0, 126.9, 126.7, 125.5, 125.0, 124.0, 75.4, 66.8, 52.0. HRMS (ESI) $[M+Na]^+$ calculated for $C_{33}H_{27}NO_3Na$ 508.1889, found 508.1884. $[\alpha]_D^{23}$ = -2490, $[\phi]_D^{23}$ = -12070 (±7%, CH_2Cl_2, 3.7 10^{-4} mol.L^{-1}).
Minor Isomer (*M,S*)-**15b**: 13 mg, mp = 103-107 °C (decomp). R_f = 0.35 (cyclohexane/AcOEt, 7/3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-7.94 (m, 7H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.82 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.60-7.57 (m, 2H), 7.44 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.18 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 6.67 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 3.52 (s, 3H), 3.51-3.43 (m, 4H), 3.42 (s, 1H), 2.00-1.96 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 133.3, 132.5, 132.3, 131.7, 131.5, 130.1, 129.8, 128.5, 128.32, 128.26, 128.14, 128.12, 128.0, 127.7, 127.6, 127.4, 127.3, 127.2, 126.9, 126.8, 126.4, 125.9, 125.5, 124.9, 124.1, 73.8, 67.0,
51.9, 50.9. HRMS (ESI) $[M+Na]^+$ calculated for $C_{33}H_{27}NO_3Na$ 508.1889, found 508.1884. $[\alpha]_D^{23}$ = -2290, $[\phi]_D^{23}$ = -11100 (±7%, CH_2Cl_2, 1.9 10^{-4} mol.L^{-1}).

ASSOCIATED CONTENT

Supporting Information
^{1}H, ^{13}C and ^{11}B spectra of compounds **9a**, **9b**, **10a**, (*P*)-**10b₁**, (*M*)-**10b₂**, **10c**, (*M*)-**12** (*M*)-**13**, (*M*)-**14** and (*M*)-**15**; X-ray diffraction data of (*M*)-**10a**, *(P)*-**10b₁** and (*M,S*)-**15b**; HPLC conditions for compounds **10a** and **10b**. This material is available free of charge on the ACS Publications website at DOI:

AUTHOR INFORMATION

Corresponding Authors
* jeanne.crassous@univ-rennes1.fr
* bertrand.carboni@univ-rennes1.fr

ORCID
Jeanne Crassous: 0000-0002-4037-6067X
Bertrand Carboni: 0000-0003-0529-715X

Notes
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