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Synthesis and characterization of new hexahelicene derivatives

Faouzi Aloui,[a] Riadh El Abed,[a] Angéla Marinetti[b] and Béchir Ben Hassine[a,*]

[a] *Laboratoire de Synthèse Organique Asymétrique et Catalyse Homogène (O1UR1201), Faculté des Sciences, Avenue de l'environnement, 5019 Monastir, Tunisia*

[b] *Institut de Chimie des Substances Naturelles, CNRS UPR 2301, Avenue de la Terrasse, 91198 Gif-sur-Yvette Cedex, France*

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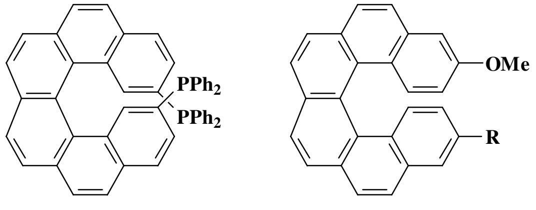
Abstract—The synthesis and structural characterization of a new hexahelicene derivative **2** is reported. This compound features a new type of structure bearing a bromine atom and a methoxy group. Suitable crystals of the latter indicate that its conformation closely resembles that of the unsubstituted [6]helicene, whose idealized symmetry is C2. This 3-bromo-14-methoxyhexahelicene was subjected to lithiation/phosphinilation and yielded the new 3-methoxy-14-(diphenylphosphino)hexahelicene **3**.

Helicenes constitute a class of polycyclic aromatic molecules derived from phenanthrene, in which the extra *ortho*-condensed rings give rise to a regular cylindrical helix due to the repulsive steric overlap of the terminal aromatic nuclei. These organic molecules present left- and right-handed chiral helical structures of *M* and *P* configuration, respectively.[1] They have been intensively studied owing to their chiroptical and nonlinear optical properties.[2] Furthermore, enantiomerically enriched helicenes have been used as chiral catalysts[3] and ligands[4] in asymmetric syntheses.

In the hexahelicene series, derivatives usually have substituents in positions 1, 2 and 15, 16 of the helicene skeleton.[5] To our knowledge, only one monodentate phosphine and one bidentate phosphine have been previously described in these series.

In an independent study, Reetz et al. described the synthesis of 2,15-bis(diphenylphosphino)hexahelicene **1** in an enantiomerically pure form (Fig. 1).[4] Its use as a helical ligand in Pd-allylic substitution confirms that it behaves as a monodentate ligand.[6] Teplý et al. prepared 3-(diphenylphosphino)hexahelicene, but they did not report a resolution or its use in catalysis.[7]



1

2: R= Br
3: R= PPh$_2$

Figure 1.

We have already described the syntheses of 3,14-dimethoxy[6]helicene and 3,14-dihydroxy[6]helicene and we have demonstrated that chelation of transition metals may be possible by these two bidentate derivatives.[8] We report here the syntheses and the crystal structure analysis of helicene **2** prepared via a Heck reaction followed by photocyclodehydrogenation.

The Heck reaction of 2-bromo-6-methoxynaphthalene **6** (2.0 g, 8.4 mmol) with 4-bromostyrene **7** (1.65 mL, 12.6 mmol) in the presence of sodium acetate and Hermann's catalyst in *N*,*N*-dimethylacetamide (20 mL) afforded diarylethene **8** in 42% yield.[9a,b] The latter was irradiated with a 150 W high-pressure mercury lamp, on a 500 mg scale, to give 2-bromo-10-methoxybenzo[*c*]phenanthrene **9** in 70% yield (Scheme 1).[10]

The Heck coupling[9a,b] of benzo[*c*]phenanthrene derivative **9** (1.0 g, 2.9 mmol) with 3-bromostyrene (1.5 equiv),

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Keywords: Hexahelicene; Heck reaction; Photodehydrocyclization; Helical phosphine; Helical alcohol.

[*] Corresponding author. Tel.: +216 73500279; fax: +216 73500278; e-mail: bechirbenhassine@yahoo.fr

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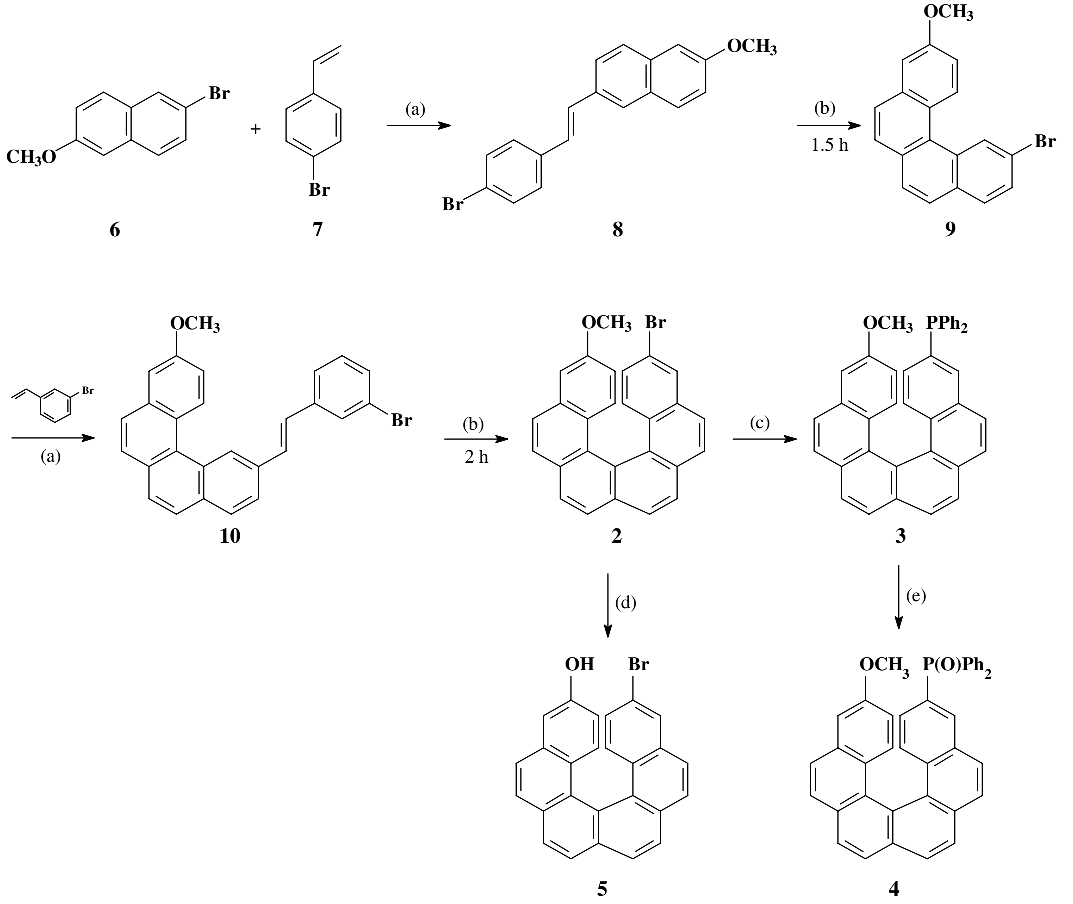
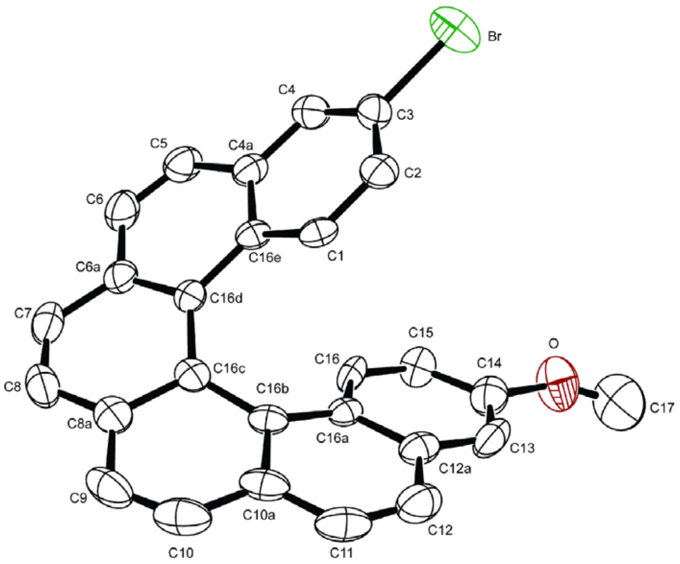


Scheme 1. Reagents and conditions: (a) Hermann's catalyst (1%), NaOAc (1.1 equiv), *N*,*N*-DMA, 140 °C, 48 h, 42% for **8**, 65% for **10**; (b) *hν*, I_2 (1.1 equiv), propylene oxide (excess), cyclohexane, 70% for **9**, 60% for **2**; (c) *n*-BuLi (1.1 equiv), THF, −78 °C, 1.5 h, then $ClPPh_2$ (1.2 equiv), −78 °C to rt, 60%; (d) BBr_3 (1.5 equiv), CH_2Cl_2, 0 °C, 3 h, 94%; (e) H_2O_2, CH_2Cl_2, rt, 30 min, 98%.

using 1% of Hermann's catalyst, produced the coupled product **10** (65% yield) possessing the *E*-stereochemistry at the double bond, based on the ^1H NMR spectrum. The photolysis of **10** was performed in cyclohexane, for about 120 min, on a 200 mg scale in the presence of a stoichiometric amount of iodine and an excess of propylene oxide[10] and afforded 3-bromo-14-methoxy-[6]helicene **2**[14] in 60% yield (Scheme 1).



Dihedral angles of **2** (°)	
C16c-C16b-C16a-C16	-11.91°
C16c-C16d-C16e-C1	-15.55°
C16e-C16d-C16c-C16b	-26.03°
C16a-C16b-C16c-C16d	-29.02°

Non bonding distances of **2** (Å)	
Br-O	6.401 Å
C(3)-C(14)	5.195 Å
C(2)-C(15)	4.172 Å
C(1)-C(16)	3.056 Å

Figure 2. Crystal structure of (±)-**2**: ORTEP drawing, selected dihedral angles (°) and nonbonding distances (Å).

Suitable crystals of compound **2** were obtained as pale-yellow plates by the slow evaporation of a methylene chloride solution. The X-ray analysis of [6]helicene **2** was carried out on a single crystal obtained from racemic **2** as shown in Figure 2. The torsion angles along the inner helical rim (C16c–C16b–C16a–C16, C16c–C16d–C16e–C1, C16e–C16d–C16c–C16b, C16a–C16b–C16c–C16d), which vary from −11.91° to −29.02°, are also a convenient measure of the helicity and are in accordance with those observed in other hexahelicenes. The terminal inner helical torsion angles 1 and 2 [C16c–C16d–C16e–C1 and C16c–C16b–C16a–C16] show somewhat unequal but relatively small opening at −15.55° and −11.91°.[15]

The demethylation of **2** using boron tribromide led to 3-bromo-14-hydroxy[6]helicene **5**[14] in 94% yield (Scheme 1).[11]

The metallation of 3-bromo-14-methoxy[6]helicene **2** was achieved by metal-halogen exchange using *n*-butyllithium at −78 °C.[12] Reaction of the lithiated species with excess chlorodiphenylphosphine yielded the desired 3-methoxy-14-(diphenylphosphino)[6]helicene **3**[14] in 60% yield, after chromatography under argon. The solid was stable to brief exposure to air and light.

Helical phosphine **3** was converted to its corresponding phosphine oxide **4**, in an excellent yield (98%), using a 35% hydrogen peroxide solution.[13] Compound **4** is more stable than phosphine **3** and could be resolved using chiral HPLC.

In summary, we have prepared and characterized, in racemic form, a new class of hexahelicene derivatives unsymmetrically disubstituted at positions 3 and 14.

3-Methoxy-14-(diphenylphosphino)hexahelicene **3** could serve as a P–O bidentate ligand in asymmetric synthesis. Its resolution is under investigation in our laboratory.

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14. Selected spectroscopic data: 3-Bromo-14-methoxyhexahelicene **2**: pale yellow solid; mp = 268–270 °C; R_f 0.29 (cyclohexane/ethyl acetate 98:02); ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 3.88 (s, 3H, OCH_3), 6.42 (dd, *J* = 2.7, *J* = 9.3 Hz, 1H, H-15), 6.81 (dd, *J* = 2.4, *J* = 9.3 Hz, 1H, H-2), 6.21 (d, *J* = 2.7 Hz, 1H, H-13), 7.50 (d, *J* = 8.7 Hz, 1H, H-16), 7.52 (d, *J* = 7.8 Hz, 1H, H-1), 7.81 (d, *J* = 8.4 Hz, 1-H), 7.87 (d, *J* = 8.7 Hz, 1-H), 7.92- 7.98 (m, 6H), 8.01 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 55.6 (OCH_3), 107.5 (C-13), 116.2 (C-15), 119.8 (C-3), 123.9 (C), 124.8 (C), 126.3 (CH), 127.0 (CH), 127.1 (CH), 127.5 (CH), 127.6 (CH), 127.8 (CH), 127.9 (CH), 128.0 (CH), 128.1 (C-2), 128.2 (C), 128.4 (C), 128.8 (C), 129.5 (C-16), 129.7 (C-1), 130.0 (CH), 130.6 (C), 131.4 (C), 133.4 (C), 133.7 (2C), 157.6 (C-14); MS (EI): $m/z = 437$ $[M^+]$. Anal. Calcd for $C_{27}H_{17}BrO$: C, 74.15; H, 3.92. Found: C, 74.10; H, 3.83.
    3-Methoxy-14-(diphenylphosphino)hexahelicene **3**: pale yellow solid, showing a violet fluorescence when dissolved; R_f 0.34 (cyclohexane/ethyl acetate 60:40); ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.95 (s, 3H, OCH_3), 6.53 (dd, *J* = 3, *J* = 9 Hz, 1H, H-2), 6.70 (ddd, *J* = 1.5, *J* = 6.5 Hz, *J* = 9 Hz, 1H, H-15), 7.22 (d, *J* = 3 Hz, 1H, H-4), 7.23–7.45 (m, 10H, 2Ph), 7.53 (d, *J* = 9 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.82–7.86 (m, 3H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 1H), 7.94–7.98 (m, 3H), 8.01 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 55.1 (OCH_3), 106.9 (C-4), 115.8 (C-2), 123.8 (C), 124.7 (C), 125.9 (CH), 126.6 (CH), 126.8 (CH), 127.1 (CH), 127.2 (CH), 127.4 (2CH), 127.6 (C), 127.7 (2CH), 127.8 (C), 128.1 (C), 128.3 (C-H), 128.5 (3CH), 128.6 (CH), 128.7 (CH), 129.1 (d, *Jcp* = 15.4 Hz, CH), 129.4 (CH), 130.1 (d, *Jcp* = 7.4 Hz, C), 131.5 (C), 131.6

(C), 131.7 (C), 133.2 (C), 133.3 (CH), 133.6 (CH), 133.7 (CH), 133.6 (d, *Jcp* = 22.0 Hz, CH), 134.0 (CH), 134.1 (d, *Jcp* = 10.0 Hz, C), 137.0 (d, *Jcp* = 10.20 Hz, C), 137.5 (d, *Jcp* = 10.65 Hz, C), 157.2 (C-14); ^{31}P NMR (202 MHz, $CDCl_3$): δ (ppm)—5.62 (s); MS (ES+): $m/z = 543.2$ $[M+H]^+$.

3-Bromo-14-hydroxyhexahelicene **5**: light-yellow solid; mp = 230–232 °C; R_f 0.21 (cyclohexane/ethyl acetate 90:10); ^{1}H NMR (300 MHz, acetone-d_6): δ (ppm) 6.39 (dd, $J = 3$, $J = 9.5$ Hz, 1H, H-15), 6.88 (dd, $J = 2$, $J = 9$ Hz, 1H, H-2), 7.29 (d, $J = 3$ Hz, 1H, H-13), 7.42 (d, $J = 9.5$ Hz, 1H, H-16), 7.55 (d, $J = 9$ Hz, 1H, H-1), 7.89 (d, $J = 8.5$ Hz, 1H), 7.99 (d, $J = 8.5$ Hz, 1H), 8.00 (d, $J = 8.5$ Hz, 1H), 8.05 (d, $J = 8.5$ Hz, 1H), 8.07–8.15 (m, 5H), 8.59 (s, 1H, OH); ^{13}C NMR (75 MHz, acetone-d_6): δ (ppm) 110.3 (C-13), 115.9 (C-15), 118.8 (C-3), 123.1 (C), 123.6 (C), 125.6 (CH), 126.5 (CH), 126.6 (CH), 127.1 (CH), 127.3 (CH), 127.4 (CH), 127.5 (CH), 127.6 (C), 127.7 (2CH), 127.9 (C), 128.5 (C), 128.9 (CH), 129.2 (CH), 129.6 (CH), 130.1 (C), 131.2 (C), 133.4 (C), 133.5 (C), 134.0 (C), 155.2 (C-14); MS (EI): $m/z = 423$ $[M^+]$.

15. Crystal data for $C_{27}H_{17}BrO$ were recorded on a Nonis MACH3/CAD4 diffractometer, $M = 437.32$, orthorhombic, *Pbca*, $a = 10.54(7)$ Å, $b = 16.563(6)$ Å, $c = 22.525(7)$ Å, $V = 3937.5(3)$ Å^3, $Z = 8$, $D_c = 1.475$ g/cm^3, X-ray source Mo Kα (radiation), $\lambda = 0.71073$ Å, $F(000) = 1776$, $T = 293(2)$ K, yellow plates $0.42 \times 0.25 \times 0.18$ mm. The structure was solved by direct methods and refined anisotropically using full-matrix least squares based on F^2 to give $R_1 = 0.0532$, $wR_2 = 0.1392$ for 4285 independent observed reflexions and 318 parameters. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 292056. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).