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Synthesis and characterization of a new hexacyclic helicene

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ABSTRACT

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Helicenes are polycyclic aromatic hydrocarbons composed of *ortho*-fused aromatic rings resulting in helical chiral and highly conjugated structures. Their specific chiral structure is due to the repulsive steric interactions between the terminal aromatic rings resulting in left and right-handed chiral helical structures of M and P configurations, respectively.¹ They exhibit specific optical rotation depending on the gross structure, and fine geometry and electronic interactions.² The unique structure of helicenes makes them very stable towards acids, bases and relatively high temperature.³

Helical backbones, which combine electron delocalization and non-planarity of the π -electron network, demonstrate various properties and applications such as circularly polarized luminescence,^{4,5} non linear optical⁶ and the ability to act as potentially useful components in chiral discotic liquid crystalline materials,⁷ as building blocks for helical conjugated polymers⁸ and as rotors.⁹ In particular, functionalized hexahelicenes and larger [*n*]helicenes are promising candidates for chiral catalysts¹⁰ and ligands¹¹ in asymmetric syntheses because of their rigid framework, high optical stability and resistance to isomerization.

The preparation of heterohelicenes has been studied extensively in order to exploit the particular properties of these helically shaped molecules. However, most of the strategies adopted for their synthesis suffer from a lack of general applicability and low yields. A few reports have described the synthesis of oxygen-containing helicenes with applications in some branches of chemistry.

In an independent study, Tepl et al. reported the synthesis of 2hydroxyhexahelicene using a route based on a key intramolecular [2+2+2] cycloisomerization of a substituted triyne.¹² The authors did not report the resolution of this helical alcohol or its use in catalysis. The first enantiomerically-enriched helical alcohol with a [6]helicene skeleton, named HELIXOL, was prepared by Reetz and Sostmann and used as an enantioselective fluores-cent sensor.¹³ Shortly after, Wachsmann et al.¹⁴ prepared 2, 15-dihydroxymethyl[6]helicene, the resolution of which was

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A new helically chiral hexacyclic system, bearing an acetoxymethyl group, was prepared from a simple

naphthalene building block in good yield and purity, via a four-step sequence involving palladium-

catalysed Heck couplings and oxidative photocyclizations. Suitable crystals of the latter indicate that

its conformation closely resembles that of unsubstituted [6]helicene, whose idealized symmetry is C₂.

The optical properties of the hexacyclic helicene were investigated and show interesting behaviour.

achieved by chiral HPLC. We have previously reported the synthesis and characterization of some interesting helically chiral aromatic structures,¹⁵ using palladium-promoted Mizoroki–Heck coupling reactions and classical oxidative photocyclization, while searching for new chiral ligands. Due to the small number of oxygen-containing [6]helicenes, we wanted to extend the same approach to the design and synthesis of a heterohelicene with an acetoxymethyl group at a selected position on the terminal aromatic group. Our synthetic strategy makes use of benzo[c]phenanthrene **1** as a key building block for the preparation of the helicene-precursor **2**. The precursor is then easily converted into the corresponding helically chiral hexacyclic system **3** by oxidative photocyclization. The acetoxymethyl group in this chiral compound serves as an appropriate functional group for increasing the solubility of the helicene in organic solvents.

The synthetic route to the helical compound **3** began with the coupling of 2-bromonaphthalene with 4-bromostyrene via a Mizoroki–Heck reaction in the presence of sodium acetate and Herrmann's palladacycle {*trans*-di(μ -acetato)-bis[o-(di-o-toly-lphosphino)-benzyl]dipalladium} as the catalyst, in *N*,*N*-dimethylacetamide (DMA). The mixture was heated at 140 °C for about 48 h to afford the corresponding diarylethene **4** in 65% yield (Scheme 1). No product of homo-coupling of 4-bromostyrene was evident. Previously, we demonstrated that the coupling reaction between 2-vinylnaphthalene and 1,4-dibromobenzene, using Heck conditions, produced the same olefin **4** in good yield.¹⁶ The resulting





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Scheme 1. Synthesis of 2-bromobenzo[*c*]phenanthrene (1).



Scheme 2. Synthesis of 2-hydroxymethylhexahelicene (5).



Figure 1. Crystal structure (ORTEP) of (±)-2-acetoxymethylhexahelicene (3).

Table 1

Selected inner and outer bond lengths (Å) and distances between non-bonded atoms in $(\pm)\textbf{-3}$

Inner C–C bond lengths	
C1-C16E	1.412
C16D-C16E	1.448
C16C-C16D	1.442
C16B-C16C	1.453
C16A-C16B	1.447
C16-C16A	1.406
Outer C–C bond lengths	
C3-C4	1.356
C5-C6	1.332
C7–C8	1.323
C9–C10	1.346
C11-C12	1.350
Distance between non-bonded atoms	
C1-C16	3.108
C2-C15	4.288
C3-C14	5.300

Table 2					
Torsion	angles	of (±)-3	and	hexaheli	cene

Compound	Torsion angle (°) ^a			
	φ1	φ2	φ3	φ4
3	15.2	29.0	14.6	26.3
Hexahelicene	11.2	30.0	15.2	30.3

^a φ1 = C16-C16A-C16B-C16C; φ2 = C16A-C16B-C16C-C16D; φ3 = C16C-C16D-C16E-C1; φ4 = C16B-C16C-C16D-C16E.

alkene **4** was subjected to photocyclization in cyclohexane using a 500 W high-pressure mercury immersion lamp. The photolysis was carried out on 800 mg scale per run in a reactor containing cyclohexane (1.5 L), for about 2 h in the presence of iodine as an oxidizing agent and excess propylene oxide as a hydrogen iodide scavenger¹⁷ to provide the expected 2-bromobenzo[*c*]phenan-threne (**1**) in 80% yield, after purification by column chromatography (Scheme 1).

Having obtained the key building block **1**, we were able to complete the convergent synthesis of the acetoxymethylhexahelicene **3**. Thus, benzo[*c*]phenanthrene **1** and 4-acetoxymethylstyrene (1.5 equiv) underwent a Mizoroki–Heck coupling using 1% of Hermann's catalyst. The desired coupled product **2**, possessing *E*-stereochemistry at the double bond, based on the ¹H NMR spectrum,¹⁸ was obtained in 75% yield after heating for 48 h at 140 °C (Scheme 2).

Alkene **2** underwent photocyclization in the presence of a stoichiometric amount of iodine and an excess of propylene oxide. The photolysis was performed on 350 mg scale per run, in a one litre

ľa	b	le	3	

Physical properties of the helically chiral compounds **3** and **5**

Compound	λ_{\max}^{Abs} (nm)	Eg (eV)
3	269	3.18
5	264	3.30

reactor for about 150 minutes to afford the expected 2-acetoxymethylhexahelicene **3** in 88% yield, and overall 34% yield (Scheme 2).¹⁹ No other regioisomer was isolated from the reaction mixture indicating that ring-closure of the diarylethene **2** had occurred at the *peri* position of the tetracyclic moiety. Treatment of compound **3** with potassium hydroxide solution (3 M) provided 2-hydroxymethylhexahelicene **5** in 98% yield (Scheme 2).²⁰

Suitable crystals of 2-acetoxymethylhexahelicene **3** were obtained as pale yellow plates by slow evaporation of a methylene chloride solution at room temperature. X-ray analysis of helicene **3** was carried out on a single crystal obtained from the racemic form as shown in Figure 1. The outer bonds C(5)-C(6), C(7)-C(8), C(9)-C(10) and C(11)-C(12) are shortened to 1.32-1.35 Å with respect to the averaged bond length in benzene (1.39 Å), whereas the inner bond distances C(1)-C(16E), C(16D)-C(16E), C(16C)-C(16D), C(16B)-C(16C), C(16A)-C(16B) and C(16)-C(16A) are lengthened to 1.40-1.45 Å (Table 1).

The torsion angles along the inner helical rim (C16–C16A–C16B–C16C, C16C–C16D–C16E–C1, C16B–C16C–C16D–C16E, C16A–C16B–C16C–C16D), which vary from 14.6° to 29.0°, are also a convenient measure of the helicity and are in accordance with those observed in hexahelicene (Table 2).²¹ The terminal inner helical torsion angles (C16–C16A–C16B–C16C and C16C–C16D–C16E–C1) show somewhat unequal, but relatively small widening at 15.2° and 14.6°.²²

The UV/vis absorption spectra of dilute helicene solutions in chloroform $(1.5 \times 10^{-6} \text{ M})$ are shown in Figure 2. The samples show strong absorption below 400 nm. The absorption of hexahelicene **3** in the high energy region is well structured containing three prominent bands at 268, 322 and 336 nm, respectively. These absorption bands are associated with π - π transitions²³ and are similar to the characteristic vibration patterns of other helicene derivatives.⁶ No broad absorption band in the low energy region was observed.

The optical band gap (Eg) determined from the absorption edge of the solution spectra is given in Table 3. The optical energy band gap of the hexahelicene **3** was calculated as 3.18 eV from the onset of the absorption around 389 nm.

In conclusion, we have prepared a new hexahelicene derivative starting from readily available and inexpensive materials. We completed the synthesis of the helical framework of **3** in only four steps with an overall 34% yield. The optical resolution of **3** is



Figure 2. UV/vis absorption spectra of the helically chiral compounds 3 and 5 in dilute $(1.5 \times 10^{-6} \text{ M})$ chloroform solutions.

currently in progress for the examination of this compound as a ligand or for broader exploitation.

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- Spectroscopic data for the diarylethene 2: colourless solid, showing violet fluorescence when dissolved in CH₂Cl₂ or CHCl₃; R_f = 0.33 (cyclohexane/EtOAc, 80:20); mp = 146–148 °C; ¹H NMR (300 MHz, CDCl₃): δ (ppm): 2.14 (s, 3H, CH₃), 5.15 (s, 2H, CH₂), 7.30 (d, J = 16.2 Hz, 1H, H_{vinyl}), 7.39–7.45 (m, 3H), 7.60–7.63 (m, 2H), 7.65–7.70 (m, 1H), 7.73–7.79 (m, 1H), 7.81–7.94 (m, 5H), 8.01 (d, J = 8.4 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ (ppm): 21.07 (CH₃), 66.11 (OCH₂), 123.21 (CH), 125.93 (CH), 126.72 (CH), 126.74 (2CH), 126.88 (CH), 126.88 (CH), 127.14 (CH), 127.26 (CH), 127.38 (C), 127.62 (CH), 130.34 (C), 130.64 (C), 131.37 (C), 133.14 (C), 133.58 (C), 135.02 (C), 135.32 (C), 137.47 (C), 170.90 (CO); HRMS (MALDI-TOF) calcd for C₂₉H₂₂O₂ [M]*: 402.16198, found:
- 19. Spectroscopic data for the 2-acetoxymethylhexahelicene **3**: pale yellow solid; $R_f = 0.35$ (cyclohexane/EtOAc, 80:20); mp = 198-200 °C; ¹H NMR (300 MHz, CDCl₃): δ (ppm): 1.93 (s, 3H, CH₃), 4.44 (d, J = 12.6 Hz, 1H, CH₂), 4.59 (d, J = 12.6 Hz, 1H, CH₂), 6.68 (ddd, $J_1 = 1.5$ Hz, $J_2 = 6.9$ Hz, $J_3 = 8.7$ Hz, 1H), 7.19– 7.26 (m, 2H), 7.57 (d, J = 8.4 Hz, 1H), 7.59 (s, 1H), 7.81 °C, 38.7 Hz, 1H), 7.91– 8.05 (m, 8H); ¹³C NMR (75 MHz, CDCl₃): δ (ppm): 20.93 (CH₃), 66.00 (OCH₂), 124.10 (C), 124.60 (CH), 125.15 (CH), 125.59 (CH), 126.26 (CH), 126.66 (CH), 126.98 (CH), 127.15 (CH), 127.24 (CH), 127.36 (2CH), 127.51 (3CH), 127.83 (C), 127.87 (C), 131.85 (C), 132.24 (C), 133.16 (C), 170.60 (CO); ESI-MS: m/z = 400.14 [M⁺]; Anal. Calcd for C₂₉H₂₀O₂: C, 86.98; H, 5.03. Found: C, 86.91; H, 5.01.
- 20. Spectroscopic data for the 2-hydroxymethylhexahelicene **5**: pale-yellow solid; $R_f = 0.20$ (cyclohexane/EtOAc, 80:20); mp = 134-136 °C; ¹H NMR (300 MHz, CDCl₃): δ (ppm): 3.95 (d, J = 12.3 Hz, 1H, CH₂), 4.12 (d, J = 12.3 Hz, 1H, CH₂), 6.68 (ddd, $J_1 = 1.2$ Hz, $J_2 = 6.9$ Hz, $J_3 = 8.1$ Hz, 1H), 7.20-7.28 (m, 2H), 7.52 (s, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.90-8.05 (m, 8H); ¹³C NMR (75 MHz, CDCl₃): δ (ppm): 65.73 (OCH₂), 124.12 (C), 124.65 (CH), 125.27 (CH), 125.48 (CH), 126.55 (CH), 126.70 (CH), 126.83 (CH), 127.21 (CH), 127.23 (CH), 127.31 (CH), 127.33 (CH), 127.44 (CH), 127.62 (C), 127.67 (2CH), 127.75 (C), 128.11 (CH), 128.35 (CH), 129.53 (C), 130.05 (C), 131.40 (C), 131.55 (C), 131.60 (C), 131.67 (C), 133.25 (C), 137.34 (C); ESI-MS: m/z = 359.1 [M+H]⁺; HRMS (MALDI-TOF) Calcd for C₂₇H₁₉O [M+H]⁺: 359.13576. Found: 359.13489.
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- 22. Crystal data for compound **3** ($C_{29}H_{20}O_2$) were recorded on a Bruker SMART CCD diffractometer, M = 400.45, triclinic, space group P-1. a = 9.2722(12) Å, b = 10.6879(14) Å, c = 23.532(3) Å, V = 2079.4(5) Å³, Z = 4, $\rho_{calcd} = 1.279$ g/ cm³, X-ray source CuK α , $\lambda = 1.54187$ Å, T = 293(2) K, measured reflections = 7067, independent reflections = 2479, reflections used = 7067. The structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 778370. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk.
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