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Synthesis of a new N-containing hexahelicene

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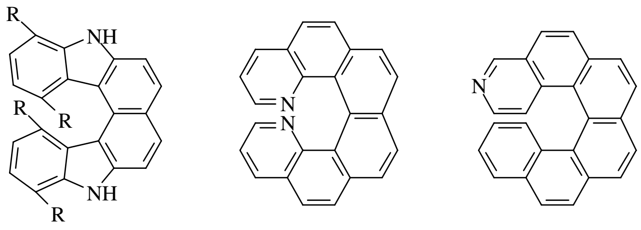
Abstract

A new helically chiral hexacyclic system, containing one pyridine unit, was prepared through a four-step synthesis involving palladium promoted Mizoroki–Heck couplings and classical oxidative photodehydrocyclisation.

Keywords: Helicenes; Heck reaction; Photodehydrocyclisation

Helicenes are a class of inherently chiral molecules constituted of *ortho*-fused aromatic rings. Their specific chiral structure, which combines electron delocalisation and non planarity of the π-electron network, is a consequence of the repulsive steric interaction between terminal aromatic rings. These helically-shaped molecules exhibit extraordinary electronic and unique chiroptical properties, for example, large circular dichroism spectra and large optical rotations.[1] Furthermore, enantiomerically-enriched helicenes have been used as building blocks for helical conjugated polymers,[2] helical ligands,[3] structures that act as catalysts[4] for enantioselective transformations and as asymmetric inducers.[5]

During the past few years, significant progress has been made in the discovery of new chiral heterohelicenes, which are promising candidates for chiral auxiliaries and chiral derivatising agents for various asymmetric reactions.[6] However, only a few examples of aza[6]helicenes have been elaborated, and methods with general applicability for syntheses of such compounds are rare. The first to be described was the pyrrolo[6]helicene **1** prepared, in racemic form, by Fuchs and Niszel via a nonphotochemical approach (Fig. 1).[7] Following the same preparative pathway, Pischel et al. reported the synthesis of the corresponding tetramethyl derivative **2** in a very poor yield and succeeded in separating its antipode using chiral HPLC.[8] Finally, Staab et al. described the synthesis of 1,16-diaza[6]helicene **3**, but they did not report its resolution.[9]



1: R = H
2: R = Me

3

4

Fig. 1.

In this Letter, we report the synthesis of a new helically chiral hexacyclic system **4**, containing one pyridine unit, through a synthetic sequence relying on Mizoroki–Heck coupling and oxidative photodehydrocyclisation reactions. The same strategy has been applied to the synthesis of various functionalised helical alcohols and helical phosphines.[10] In this work, our synthetic procedure makes use of 2-bromobenzo[*c*]phenanthrene **6** as a starting material for the synthesis of helicene-precursor **7**, which is then converted easily to the corresponding nitrogen-containing hexahelicene **4** by photolysis. The nitrogen atom in this

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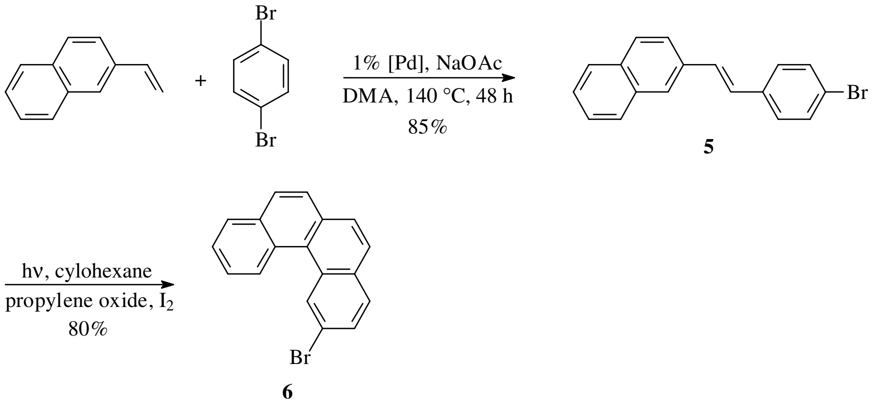


Scheme 1. Synthesis of 2-bromobenzo[*c*]phenanthrene **6**.

chiral helicene could serve as a hydrogen acceptor as well as a metal chelating agent for chirality recognition.

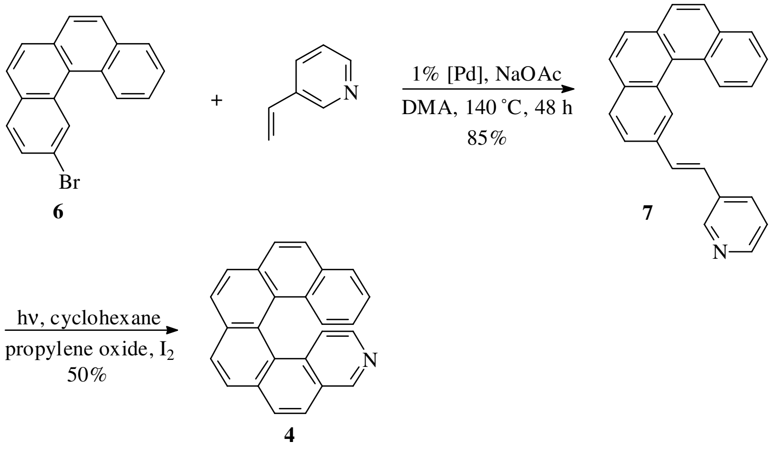
The synthetic route to aza[6]helicene **4** began with the coupling of 2-vinylnaphthalene and 1,4-dibromobenzene through a Mizoroki–Heck coupling reaction[11] according to the following conditions: 1% of Hermann's palladacycle [*trans*-di(μ-acetato)-bis[*o*-(di-*o*-tolylphosphino)benzyl]-dipalladium] as the catalyst, sodium acetate as the base and *N*,*N*-dimethylacetamide (DMA) as the solvent. The mixture was heated at 140 °C for about 48 h to afford the desired styryl derivative **5** (85% yield) possessing *E*-stereochemistry at the double bond, based on the ^{1}H NMR spectrum (Scheme 1). The resulting alkene **5** was subjected to photocyclisation in cyclohexane for about 2 h in the presence of iodine using a 150 W high-pressure mercury immersion lamp to provide the expected 2-bromobenzo[*c*]phenanthrene **6** in an 80% yield, after purification by column chromatography.

The Mizoroki–Heck coupling of 2-bromobenzo[*c*]phenanthrene **6** with 3-vinylpyridine in the presence of sodium acetate and Hermann's catalyst in *N*,*N*-dimethylacetamide afforded the helicene precursor **7** in 85% yield, after purification by column chromatography, with a total of 58% yield over three steps (Scheme 2). The final step of the synthetic approach is formation of the helical framework, which could be achieved through oxidative photocyclisation of compound **7**. The latter was irradiated on a 200 mg scale per run in cyclohexane, in the presence of iodine as an oxidating agent and an excess of propylene oxide as a hydrogen iodide scavenger,[12] to afford the expected 3-azahexahelicene **4**[13] in 50% yield (29% overall yield) (Scheme 2).

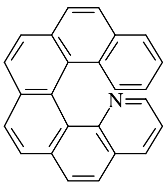
For the photoconversion of larger amounts of the olefin derivative **7** it was preferable to carry out the irradiation using portions of 0.6 mmol or less of the reactant. The total irradiation time required for the complete conversion of a large amount of **7** was not affected significantly by dividing the reactant into small batches, and the irradiated batches could be combined for work-up.

The ring closure of olefin **7** was not completely regioselective since 1-azahexahelicene **8** was isolated in 7% yield and identified as a minor, helically chiral, compound in the reaction mixture (see Fig. 2).[14] Heterohelicenes **4** and **8** were successfully separated by column chromatography.

In summary, we have described a straightforward method to prepare the helically chiral framework of the hexacyclic system **4** using a repetitive Mizoroki–Heck reaction/photodehydrocyclisation tandem methodology. We



Scheme 2. Synthesis of 3-azahexahelicene **4**.



8

Fig. 2. Structure of helically chiral compound **8**.

completed the synthesis of the aza[6]helicene in only four steps with an overall 29% yield. Work is now in progress to extend this method to the preparation of various functionalised aza[6]helicenes.

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13. *Selected spectral data for 3-azahexahelicene* **4**: Light yellow solid, showing a violet fluorescence when dissolved in methylene chloride; R_f 0.25 (cyclohexane/ethyl acetate 70:30); mp: 278–280 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 6.74 (t, $J = 7.5$ Hz, 1H, H-14 or H-16), 7.28 (m, 2H), 7.53 (d, $J = 8.7$ Hz, 1H), 7.77 (d, $J = 6$ Hz, 1H), 7.87 (d, $J = 8.1$ Hz, 1H), 7.93–8.01 (m, 6H), 8.04 (d, $J = 8.7$ Hz, 1H), 8.09 (d, $J = 8.1$ Hz, 1H), 9.20 (s, 1H, H-4); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 120.07 (CH), 124.18 (C), 125.31 (CH), 126.15 (3CH), 126.25 (C), 126.53 (C), 126.98 (CH), 127.20 (CH), 127.33 (CH), 127.91 (C and CH), 127.95 (2CH), 128.48 (CH), 129.00 (CH), 129.88 (C), 131.73 (C), 131.81 (C), 133.15 (C), 133.19 (C), 133.80 (C), 142.83 (CH), 151.44 (CH); MS (EI, 50 eV): $m/z = 330$ ($[M+H]^+$, 100%), 329 ($M^{+\cdot}$, 92%); Anal. Calcd for $C_{25}H_{15}N$: C, 91.16; H, 4.59; N, 4.25. Found: C, 91.06; H, 4.57; N, 4.21.
14. *Selected spectral data for 1-azahexahelicene* **8**: Yellow solid; R_f 0.50 (cyclohexane/ethyl acetate 80:20); mp: 189–191 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 6.61 (t, $J = 8.1$ Hz, 1H), 7.12 (dd, $J = 4.2$, 8.1 Hz, 1H, H-3), 7.21 (t, $J = 7.8$ Hz, 1H), 7.58 (d, $J = 8.4$ Hz, 1H), 7.87 (m, 2H), 7.91–7.97 (m, 3H); 8.00–8.07 (m, 4H), 8.13 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 120.69 (C-3), 124.26 (CH), 124.80 (CH), 126.13 (CH), 126.19 (CH), 126.33 (CH), 126.40 (C and CH), 126.64 (CH), 127.35 (CH), 127.62 (C and CH), 127.98 (CH), 128.26 (CH), 128.63 (C), 128.73 (CH), 129.78 (C), 131.09 (C), 131.24 (C), 131.85 (C), 133.17 (C), 133.37 (C), 135.33 (CH), 145.78 (C), 146.77 (CH); ESI-MS: $m/z = 330.1$ $[M+H]^+$; Anal. Calcd for $C_{25}H_{15}N$: C, 91.16; H, 4.59; N, 4.25. Found: C, 91.04; H, 4.55; N, 4.23.