

First expeditious synthesis of 6,11-diamino-[6]carbohelicenes†

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The first synthesis of 6,11-diamino-[6]carbohelicenes is described: the short 5 step sequence involves Suzuki–Miyaura coupling, functional group transformations and electrophilic aromatic cyclisation; the original strategy allows the preparation of di- and tetra-substituted helicenes in comfortable yields.

Helicenes are helically shaped fascinating molecules. Known for more than 100 years, these aromatic non-planar molecules have attracted continual interest. In the last decade, the scientific community has discovered the extraordinary optical and electronic properties of helicenes,¹ which has revived synthetic efforts to provide really convenient preparation methods.²

Among carbohelicenes, [6]carbohelicenes, which refer to six consecutive *ortho*-fused benzene rings, are one of the most studied. The key step of their preparation is the construction of the last ring(s) that allows the final assembly and aromatisation. For example, formation of rings 3 and 4 (Scheme 1, strategy a), was the key step of Newman and Lednicer's first reliable synthesis of [6]carbohelicene.³

Since then [6]carbohelicenes have been classically prepared by photocyclisation of bis(stilbenes) (strategy b).⁴ Recently, the need for variously substituted helicenes has led to the development of several other appealing approaches. Indeed, Katz *et al.*⁵ described an elegant access to helicene bisquinone derivatives through a Diels–Alder strategy (route c). Further original strategies involve transition metal-catalysed [2 + 2 + 2]-cycloisomerisation of triynes or dienetriynes (strategy d),^{2d,6} olefin metathesis (strategy e),^{2c,7} intramolecular Pd-catalysed C–C bond formation (strategy f)⁸ or Friedel–Crafts cyclisation (strategy g).⁹ Interestingly, the nature of the substituents and the substitution pattern at the helicene core are highly dependent on the preparation method. If alkoxy groups, alkyl groups, and bromides are common substituents, access to alcohols, phosphines or amines is scarcely reported. Moreover, introduction of such valuable substituents requires further transformations on a preformed helicene.^{4,10} Despite remarkable progress in helicene chemistry, development of new, short and efficient routes that further allow direct functionalisation remains a challenge.

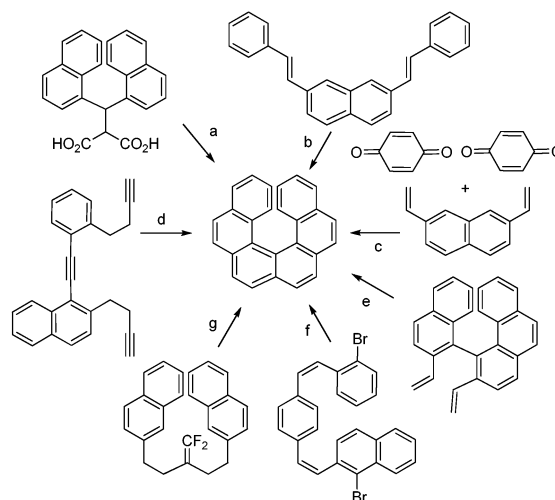
In this communication, we report an original short approach to 6,11-diamino-[6]carbohelicene, starting from commercially

available compounds as outlined retrosynthetically in Scheme 2. We assumed that target **1** should be obtained from **2** by using acidic conditions to perform the cyclisation and construction of rings 2 and 5. Compound **2** was envisioned through successive dibromination and dicyanation of compound **3**. Finally, a Suzuki–Miyaura coupling reaction carried out on **4**¹¹ should allow access to compound **3**.

Although the preparation of several 1,8-diaryl- and 1,8-diheteroarylnaphthalenes is well known,¹² their syntheses suffer from a lack of generality. This inclined us to use a phosphane free catalytic system. Indeed, 1,8-dibromonaphthalene was coupled to *o*-tolylboronic acid under Suzuki–Miyaura conditions in the presence of caesium carbonate and 1% palladium(II) complex **5**¹³ to give 1,8-di(*o*-tolyl)naphthalene **4** in 80% yield. Bromination under radical conditions,¹⁴ using NBS, AIBN in CCl₄, followed by cyanation¹⁵ of the resulting dibromo intermediate, led to the desired dinitrile **2** with a 60% yield (two steps). Finally, PPA was added to compound **2** and heated to 100 °C for 24 h.¹⁶ Those cyclisation conditions induced the simultaneous construction of two aromatic rings, providing **1** in a nearly 40% yield. For practical reasons, **1** was isolated as diacetamide derivative **6** (Scheme 3). A similar five step sequence allowed a rational access to tetrasubstituted [6]-helicene **9** in a comfortable 25% overall yield (Scheme 4).

Due to the potential instability of methoxy groups in rather highly acidic conditions, we tried to use sonoactivation in the cyclisation step. Under these mild conditions, helicene **9** was obtained in a fair 40% yield from the parent compound **8**.

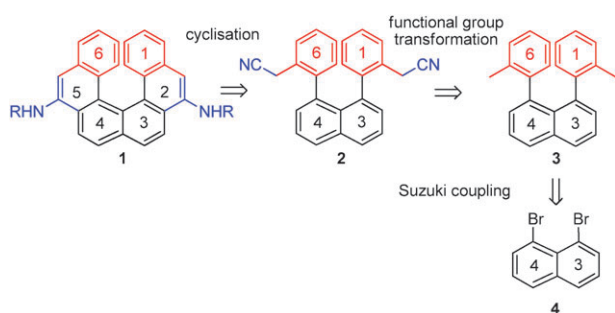
Single crystal X-ray diffraction analysis confirmed the helical structure of carbohelicene **9** (Fig. 1).



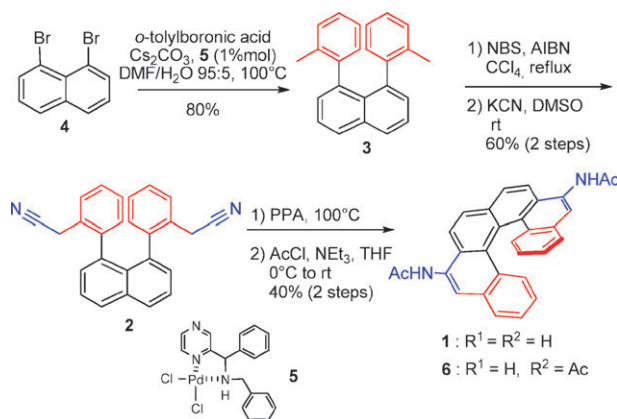
Scheme 1 Synthesis of [6]carbohelicenes.

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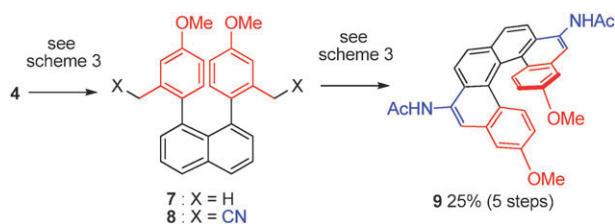
† Electronic supplementary information (ESI) available: Crystallographic data of **9** and experimental preparatins for **4**, **7**, **8** and **9**. CCDC 719176. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b905670j



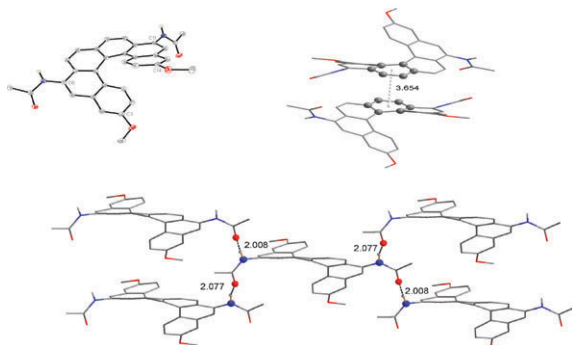
Scheme 2 Retrosynthetic approach to helicenes.



Scheme 3 Synthetic pathway to 6,11-diamino-[6]helicenes.



Scheme 4 Tetrasubstituted [6]helicene 9.

Fig. 1 Single crystal X-ray diffraction analysis of helicenes 9.¹⁷

As depicted in Fig. 1, the presence of acetamido substituents induced the formation of strong hydrogen bond nets. Within this 2D NH...O-bonded network each molecule is H-bonded to four neighbours with the same helicity. Interestingly, each molecule within a 2D net is packed in stacks of columns with consecutively opposing helicity. Within the stacks, the molecular arrangement resulted from well-defined intermolecular

π - π interactions with an average distance of 3.65 Å between rings 4 of two adjacent head-to-tail stacked molecules.

In conclusion, we have described the first synthesis of 6,11-diamino[6]-carbohelicene derivatives, in a short five step sequence. Extension of the strategy to selective preparation of polysubstituted helicenes of various sizes, is currently under investigation.

Notes and references

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- 17 Crystal data: $C_{32}H_{26}N_2O_4 \cdot C_2H_3N$, $M_w = 543.60$, triclinic, space group $P-1$; dimensions: $a = 9.4922(14)$ Å, $b = 11.5758(16)$ Å, $c = 13.5860(18)$ Å, $\alpha = 79.913(7)^\circ$, $\beta = 75.844(7)^\circ$, $\gamma = 73.560(7)^\circ$, $V = 1379.3(3)$ Å³; $Z = 2$; $\mu = 0.09$ mm⁻¹; 40 142 reflections measured at 100 K; independent reflections: 8030 [$6310 F_o > 4\sigma(F_o)$]; data were collected up to a $2\theta_{max}$ value of 60.34° (98.2% coverage). Number of variables: 375; $R_1 = 0.0469$, $wR_2 = 0.1267$, $S = 1.062$; highest residual electron density 0.447 e Å⁻³ (all data $R_1 = 0.0630$, $wR_2 = 0.1397$). CCDC 719176. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b905670j.