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TETRAHEDRON
LETTERS

[5]Helicenes by tandem radical cyclisation

David C. Harrowven,[a,]* Michael I. T. Nunn[a] and David R. Fenwick[b]

[a]*Department of Chemistry, The University of Southampton, Southampton SO17 1BJ, UK*
[b]*Discovery Chemistry, Pfizer Global Research and Development, Sandwich, Kent CT13 9NJ, UK*

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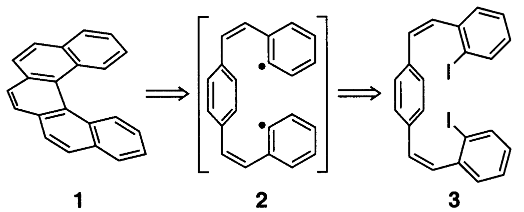
Abstract—A new and rapid approach to [5]helicenes is described. A central feature is the use of a sequential, non-reducing radical cyclisation reaction of (*Z*,*Z*)-1,4-bis(2-iodostyryl)benzene derivatives, viz. **3**→**1**, mediated by tributyltin hydride. © 2002 Elsevier Science Ltd. All rights reserved.

For many years helicenes were regarded as little more than an academic curiosity. More recently their extraordinary optical and electronic properties have rekindled an interest in these non-planar condensed aromatics in fields as diverse as liquid crystals,[1] sensors,[2] asymmetric synthesis and polymer synthesis.[3,4] Helicenes are commonly prepared by oxidative photocyclisation.[5,6] Though useful, the method can give rise to complex product mixtures due to poor regiocontrol in the photocyclisation step and competitive side reactions such as photo-induced dimerisation or benzo-[*ghi*]perylene formation.[6] Several alternative strategies have therefore been developed for the synthesis of helicenes,[7] including methods based on Diels–Alder cycloaddition reactions and carbenoid insertion reactions.[8,9]

Our interest in radical additions to aromatic and heteroaromatic ring systems,[10] prompted us to explore an alternative entry to helicenes based on a tandem radical cyclisation strategy (Scheme 1). Having shown that 6-*endo*/*exo*-trig cyclisations of aryl radicals to arenes provide a high yielding route to phenanthrenes,[11] and that related cyclisations to phenanthrenes can give helicenes,[12] it seemed likely that the two processes could be run in parallel. In this letter we report our realisation of that objective.



Scheme 1.

The first target we decided to address was the parent [5]helicene **1**. To that end, *p*-xylylene dibromide **4** was transformed into the corresponding *bis*-phosphonium salt **5** by treatment with triphenylphosphine.[6a,13] A tandem Wittig reaction was then effected with *o*-iodobenzaldehyde, giving a 1:1 mixture of (*Z*,*E*)- and (*Z*,*Z*)-1,4-bis(2-iodostyryl)benzenes **7** and **3** in 77% yield. These were readily separated by column chromatography. Pleasingly, treatment of **3** with tributyltin hydride under standard radical forming conditions, gave [5]helicene **1** in 58% yield (Scheme 2).

With the viability of the approach established, we next sought to extend the method to other [5]helicenes. A series of iodobenzaldehyde derivatives **11a**–**d** were thus prepared using standard protocols (Scheme 3). Each was then coupled to **6** to give 1,4-bis(2-iodostyryl)benzenes **12a**–**d**, respectively. In each case the major product formed was the desired (*Z*,*Z*)-isomer and this could be separated from the product mixture by a combination of column chromatography and recrystallisation. The (*Z*,*E*)-isomers were found to be significant byproducts while the (*E*,*E*)-isomers accounted for little more than 5% of the total mass balance (Scheme 3).

The stage was now set to examine the generality of the reaction in more detail. Pleasingly, each of the (*Z*,*Z*)-1,4-bis(2-iodostyryl)benzenes **12a**–**d**, gave the corresponding [5]helicene as the major product on treatment with tributyltin hydride under standard radical forming conditions (4.4 equiv. Bu_3SnH, 0.4 equiv. AIBN,

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* Corresponding author.

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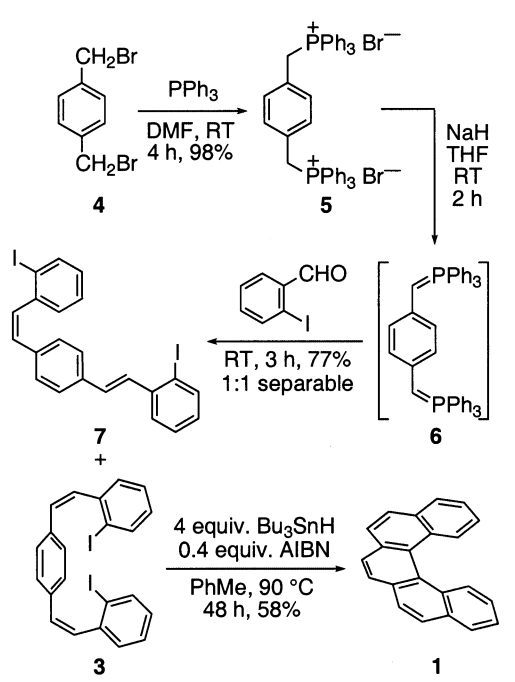
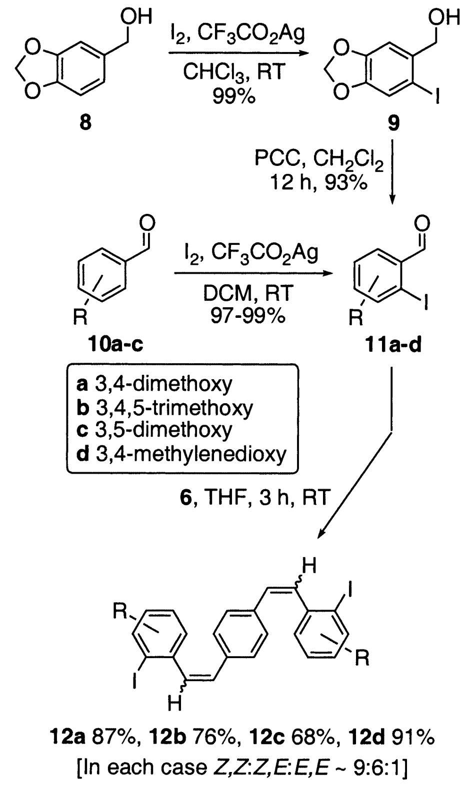


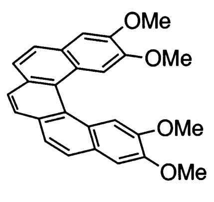
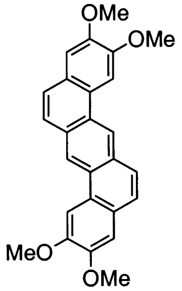
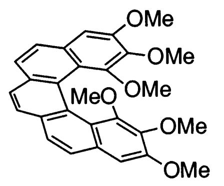
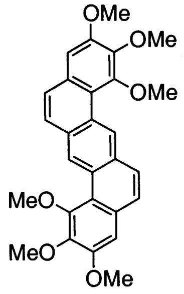
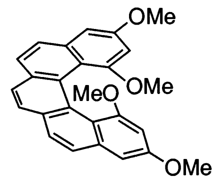
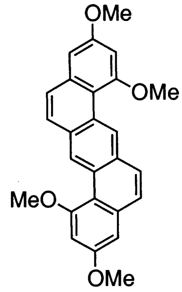
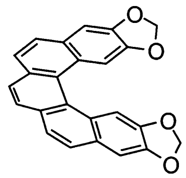
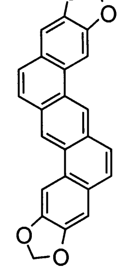
Scheme 2.



Scheme 3.

PhMe, 90°C). Yields ranged from 35 to 49% (Table 1). These helicenes were accompanied by the corresponding dibenzo[*a*,*h*]anthracene, arising from cyclisations of the aryl radical intermediates to the C2 and C5 centres of the central arene. Though these were isolated in yields ranging from 3 to 27%, they were undoubtedly formed in greater quantity—their low solubility in toluene and ethyl acetate, combined with our employment of an aqueous KF work-up procedure, led to substantial mechanical losses of these byproducts.

Table 1. Radical cyclisation reactions leading to helicenes

Substrate	[5]helicene	minor product
12a	 **13**, 40%	 **14**, 5%
12b	 **15**, 35%	 **16**, 27%
12c	 **17**, 49%	 **18**, 3%
12d	 **19**, 41%	 **20**, 14%

In conclusion, we have developed a new route to [5]helicenes based on a tin mediated, non-reducing tandem radical cyclisation of (*Z*,*Z*)-1,4-bis(2-iodostyryl)benzene derivatives. The approach is short and easy to effect, with the key step providing helicenes in 35–58% yield. We are presently seeking to extend the method to higher helicenes and related structures that are difficult to prepare by traditional methods.

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