

Efficient asymmetric synthesis of [7]helicene bisquinones†‡

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The efficient one-pot six-step domino process which occurs when (SS)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone (**1**) reacts with 3,6-divinyl-1,2,7,8-tetrahydrophenanthrenes **2a–c** allowed enantioselective access to [7]helicene bisquinones **3a–c** with excellent optical purities (96 to > 99% *ee*).

Helicenes¹ are an important group of compounds due to their extraordinary optical and electronic properties² closely associated with their inherent chirality. In recent years, several protocols have emerged for the construction of this type of polycyclic skeletons,³ which have mainly focused on [5]- and [6]helicenes, [7]helicene derivatives being less studied.

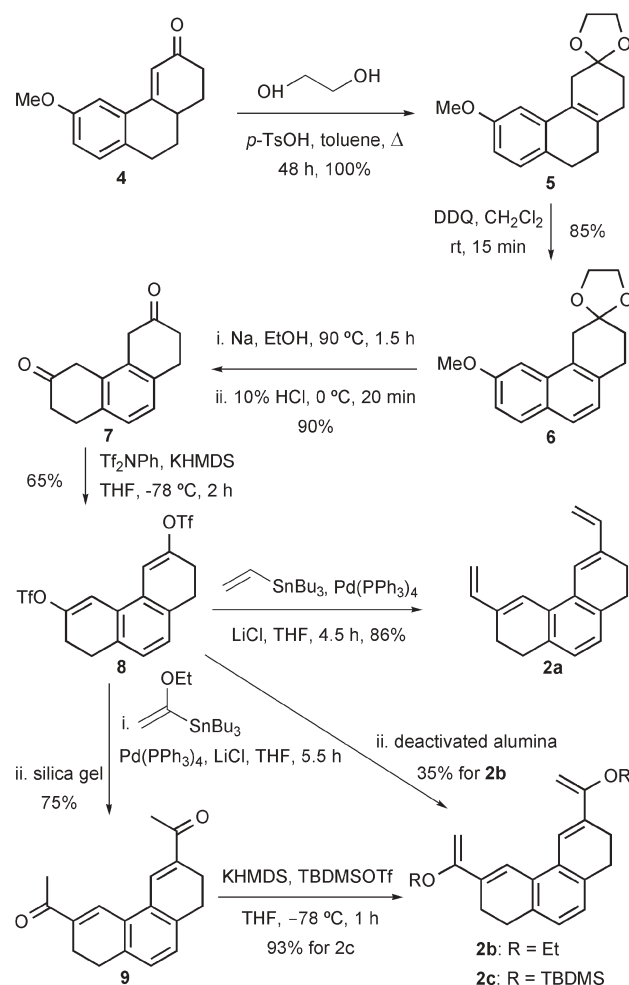
In 1967,⁴ Martin described the first synthesis of racemic heptahelicene based on the oxidative photocyclization of stilbene-type precursors.⁵ Since then, several light-mediated syntheses of [7]helicenes⁶ have been reported. More recently, new non-photochemical methodologies have been developed for the assembly of the racemic heptahelicene framework.⁷

Most of the approaches to the enantiomers of [7]helicenes described to date are based on chromatographic,⁸ enzymatic⁹ or chemical resolutions¹⁰ of the racemic derivatives. Non-racemic [7]helicene bisquinones have been synthesized by Katz on a multigram scale by chemical resolution of the products resulting from reaction between benzoquinone and aromatic silyl enol ethers.¹⁰ The few asymmetric syntheses reported, based on diastereoselective photocyclizations,¹¹ occurred with moderate selectivities, except in one case.^{11a} To the best of our knowledge, there is no enantioselective approach to [7]helicenes.

We have recently described¹² a new asymmetric synthesis of dihydro[5]helicenequinones based on the domino Diels–Alder reaction/pyrolytic sulfoxide elimination/aromatization process which occurred when vinyl dihydrophenanthrenes reacted with (SS)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone (**1**). Herein we report the first non-photochemical asymmetric access to helically chiral tetrahydro[7]helicene bisquinones (**3**) with excellent optical purities from the reaction between several 3,6-divinyl-1,2,7,8-tetrahydrophenanthrenes (**2**) and (SS)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone (**1**), giving rise to the enantiopure heptacyclic system in an efficient one-pot six-step double domino process.

Scheme 1 illustrates the preparation of *bis*-dienes **2**. Known ketone **4**¹³ was prepared in two steps from commercially available 7-methoxy- α -tetralone. Protection of **4** as a dioxolane took place with simultaneous isomerization of the double bond giving rise to

acetal **5** in quantitative yield. Treatment of **5** with DDQ led to tetrahydrophenanthrene **6** in 85% yield, after aromatization of the central ring. The 2-methoxy substituted aromatic ring of **6** was selectively reduced using sodium in refluxing ethanol and, after acidic hydrolysis of the intermediate vinyl ether and the acetal protecting group, diketone **7** was isolated in 90% yield. Successive treatment of **7** with KHMDS and Tf₂NPh afforded *bis*-triflate **8**, a common intermediate in the synthesis of dienes **2a–c** required for the preparation of the [7]helicene bisquinones **3a–c**. A double Stille coupling between **8** and tributylvinylstannane led to 3,6-divinyl tetrahydrophenanthrene **2a** in 86% yield. Using tributyl-(1-ethoxyvinyl)stannane as the coupling partner, *bis*-diene **2b**, bearing an OEt substituent at the vinyl moiety, was synthesized. Although the reaction took place with good yield, only a 35% yield

Scheme 1 Synthesis of *bis*-dienes **2a–c**.

† Electronic supplementary information (ESI) available: experimental section. See <http://www.rsc.org/suppdata/cc/b413879a/>

‡ This paper is dedicated to Dr Juan Carlos del Amo who died in the terrorist attacks which occurred in Madrid on March 11th, 2004.

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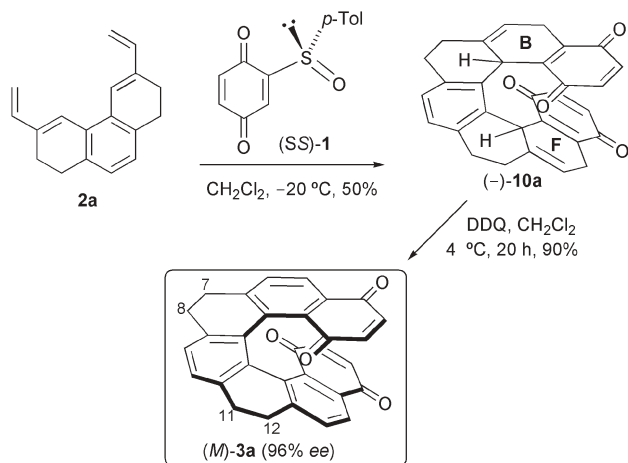
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of compound **2b** was isolated pure due to the hydrolysis of the enol ethers to the corresponding diketone **9** during chromatographic purification, even using deactivated neutral alumina as the stationary phase. Nevertheless, compound **9**, isolated in 75% yield after silica gel chromatography of crude derivative **2b**, could be transformed into a new *O*-silylated divinyl derivative **2c**, by treatment with KHMDS and TBDMSTf, in 93% yield.

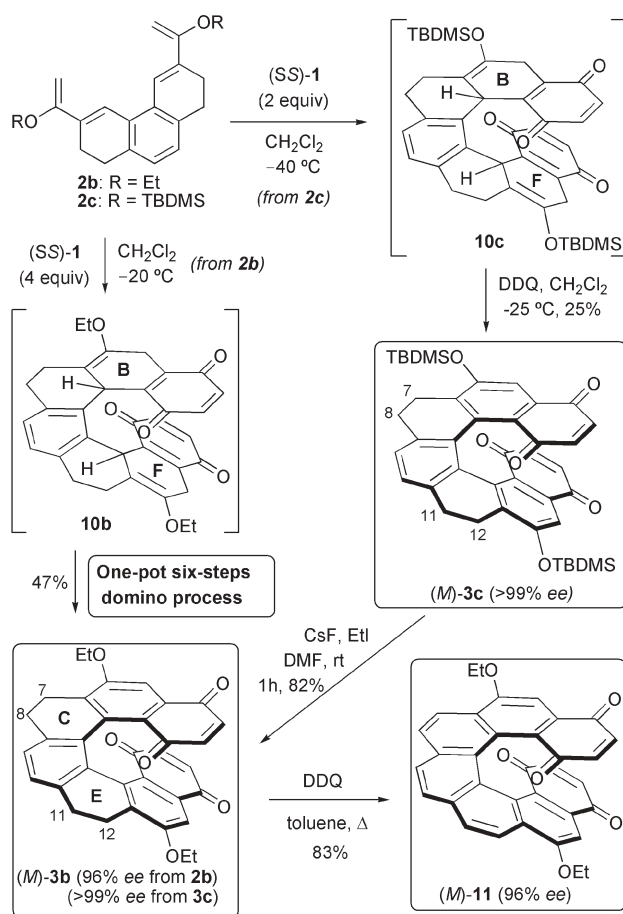
With all *bis*-dienes **2a–c** in hand, we carried out their reactions with (*SS*)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone (**1**)¹⁴ *en route* to heptacyclic bisquinones **3a–c** (Scheme 2). Diene **2a** reacted with (*SS*)-**1** at $-20\text{ }^{\circ}\text{C}$ giving the octahydroaromatic derivative **10a** $\{[\alpha]_{\text{D}}^{20} = -686$ (*c* 0.04, CHCl_3) $\}$, bearing two stereogenic centers, in 50% yield. This compound proceeded from a double domino process between (*SS*)-**1** and **2a** comprising Diels–Alder reaction and elimination of the sulfoxide in the initially formed cycloadducts. Under these conditions, we did not observe the aromatization of the hydroaromatic B and F rings of (–)-**10a**, even in the presence of an excess of (*SS*)-**1**. This transformation was later effected by treatment of (–)-**10a** with DDQ giving rise to tetrahydro[7]helicene bisquinone (*M*)-**3a** $\{[\alpha]_{\text{D}}^{20} = -5825$ (*c* 0.01, CHCl_3) $\}$, showing helical chirality,[§] in 90% yield with an excellent 96% *ee*.[¶]

The reaction between (*SS*)-**1** and diene **2b** (Scheme 3) allowed the direct synthesis of tetrahydro[7]helicene bisquinone (*M*)-**3b** $\{[\alpha]_{\text{D}}^{20} = -2938$ (*c* 0.06, CHCl_3) $\}$ (47% yield, 96% *ee*).[¶] This process occurred at $-20\text{ }^{\circ}\text{C}$ in the presence of an excess of quinone (*SS*)-**1** and took place through a one-pot six-step domino sequence including a double Diels–Alder reaction, sulfoxide elimination and aromatization of the B and F rings of octahydroaromatic intermediate **10b**. The presence of the electron donating OEt group facilitated both the cycloaddition and the aromatization process. We were also interested in performing the complete aromatization of hydroaromatic C and E rings of compound (*M*)-**3b** (96% *ee*). This transformation was achieved using DDQ in refluxing toluene obtaining the fully aromatized [7]helicene bisquinone (*M*)-**11** $\{[\alpha]_{\text{D}}^{20} = -825$ (*c* 0.08, CHCl_3) $\}$, in 83% yield and 96% *ee*[¶] (Scheme 3).

When (*SS*)-**1** and the (*tert*-butyldimethylsilyloxy)-substituted diene **2c** reacted under similar conditions to those used with **2b**, tetrahydro[7]helicene bisquinone (*M*)-**3c** was obtained with low optical yield. The optical purity of (*M*)-**3c** could be enhanced by



Scheme 2 Asymmetric synthesis of tetrahydro[7]helicenebisquinone (*M*)-**3a**.



Scheme 3 Asymmetric synthesis of tetrahydro[7]helicenebisquinones (*M*)-**3b** and (*M*)-**3c** and fully aromatized [7]helicenebisquinone (*M*)-**11**.

performing the double domino process comprising cycloaddition and sulfoxide elimination at $-40\text{ }^{\circ}\text{C}$, followed by aromatization of the B and F rings of intermediate **10c** with DDQ at $-25\text{ }^{\circ}\text{C}$. Under these conditions, enantiopure heptacyclic bisquinone (*M*)-**3c** $\{[\alpha]_{\text{D}}^{20} = -1990$ (*c* 0.02, CHCl_3) $\}$, *ee* > 99%,[¶] was obtained in 25% yield. The *O*-silylated heptahelicene (*M*)-**3c** was transformed into enantiopure derivative (*M*)-**3b** $\{[\alpha]_{\text{D}}^{20} = -3180$ (*c* 0.05, CHCl_3) $\}$, *ee* > 99%,[¶] by treatment with CsF followed by trapping with EtI, in 82% yield.

In summary, we have described the first enantioselective approach to [7]helicene derivatives based on the double domino one-pot six-step process between 3,6-divinyl-1,2,7,8-tetrahydrophenanthrenes **2**, prepared in only 5 or 6 steps from the common known ketone **4**, and (*SS*)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone (**1**). We have synthesized three new tetrahydro[7]helicene bisquinones and one fully aromatized derivative with excellent optical purities (96 to > 99%).

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Notes and references

§ The absolute configuration of the [7]helicenes was established by applying the methodology described by Katz based on the different TLC and NMR features of (*M*)- and (*P*)-helicenol camphanates.¹⁵

¶ The enantiomeric excesses were determined by chiral HPLC.

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