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Inner–outer ring 1,3-bis(trimethylsilyloxy)-1,3-dienes as useful intermediates in the synthesis of helicenes

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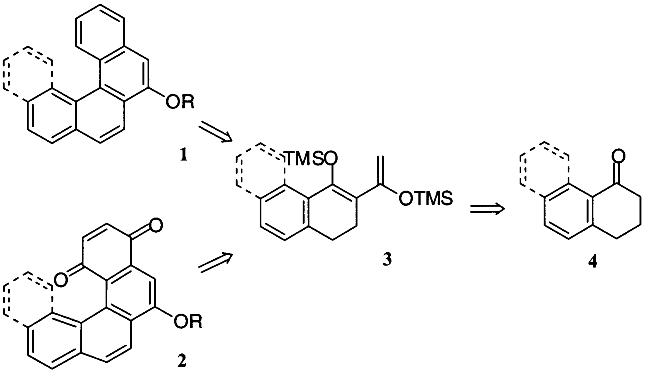
Abstract—Functionalized benzo[*c*]phenanthrenes ([4]helicenes) and [5]helicenes were synthesised in five steps from tetrahydronaphthalenone and tetrahydrophenanthrenone compounds using a novel synthetic approach based on a Diels–Alder reaction between inner–outer ring 1,3-bis(trimethylsilyloxy)-1,3-dienes and benzyne or quinones. © 2002 Elsevier Science Ltd. All rights reserved.

Helicenes,[1] helical molecules comprised of *ortho*-fused aromatic rings, are interesting compounds with potential utility as new materials such as discotic liquid crystals,[2] self-assembling corkscrew structures[3] or conjugated polymers[4] and also as chiral auxiliaries in asymmetric synthesis.[5] This unique class of compounds has been traditionally accessible through stilbene photocyclizations,[6] although during the past decade new synthetic methodologies have emerged to provide useful alternatives.[7] The synthesis of helicenes through a Diels–Alder reaction using inner–outer ring dienes such as vinyl arenes has been the most practical approach to date.[8] The main synthetic problems associated with this approach arise from the low reactivity and regioselectivity of the aromatic dienes, which led to the use of harsh reaction conditions or gave mixtures of regioisomers.[9] These problems have been overcome in some cases by using oxygenated dienes.[10]

1,3-Bis(silyloxy)dienes and related masked dianions are useful synthons in cyclization reactions.[11] In recent years we have been interested in studying the Diels–Alder reactivity of the scarcely explored inner–outer ring 1,3-bis(trimethylsilyloxy)-1,3-dienes and their utility for the synthesis of polycyclic compounds.[12] Our studies have shown that these dienes can be easily prepared from 1,3-dicarbonyl compounds and that they exhibit high reactivity and regioselectivity towards different dienophiles, generally under mild reaction conditions. In this communication we wish to report the novel use of inner–outer ring 1,3-silyloxy-1,3-dienes in the Diels–Alder reaction for the synthesis of helicenes.

The synthesis of helicenes was envisioned through a retrosynthetic approach based on a Diels–Alder reaction of an inner–outer ring 1,3-bis(trimethylsilyloxy)-1,3-diene (**3**), derived from a tetrahydroaromatic ketone (**4**), with a cyclic dienophile (Scheme 1). The size of the helicene will be determined by the cycloaddition partners; we report here the use of tetrahydronaphthalene and tetrahydrophenanthrene ketones as diene precursors and benzyne and quinones as dienophiles. The Diels–Alder reaction with benzyne would allow the direct incorporation of an extra-aromatic ring (**1**). The Diels–Alder reaction with quinones would allow the synthesis of helicenequinones (**2**), compounds with novel structural and optical properties, the synthesis of which has been largely pursued by Katz's group.[2,3]



Scheme 1.

Keywords: 1,3-bis(trimethylsilyloxy)-1,3-dienes; Diels–Alder reactions; helicenes; quinones; sulfoxides.

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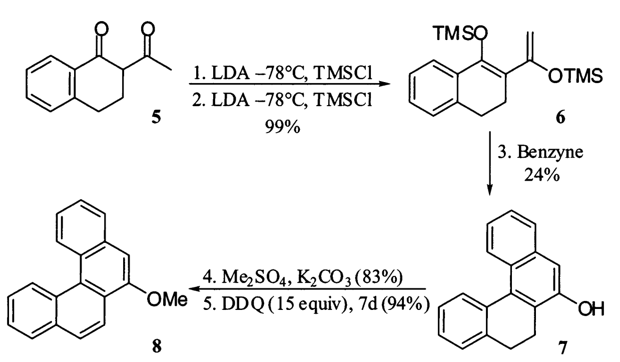
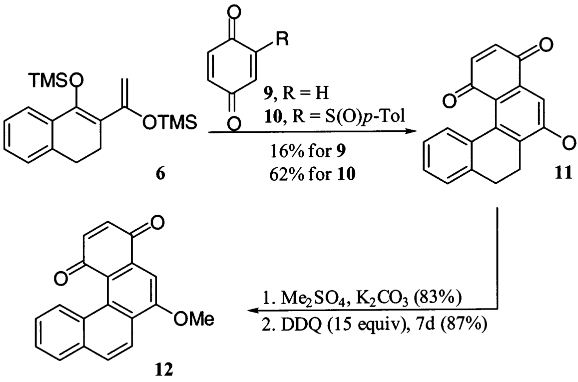
We began with the synthesis of benzo[*c*]phenanthrenes ([4]helicenes). The treatment of commercial 2-acetyl-1-tetralone (**5**) with LDA at low temperature followed by trapping of the resulting enolate with TMSCl (twice), in a sequential one-pot/two-step procedure, gave the 1,3-bis(trimethylsilyloxy)-1,3-diene **6** in quantitative yield.[†] Treatment of diene **6** with benzyne, generated by thermal decomposition of benzenediazonium 2-carboxylate,[13] at reflux in THF gave the dihydrobenzo[*c*]phenanthrenol **7** in 24% yield. Unfortunately, the silyloxydiene was hydrolyzed to some extent in the reaction medium and substantial amounts of 2-acetyl-1-tetralone (40%) were recovered. The formation of **7** involves three steps: cycloaddition, trimethylsilyl enol ether hydrolysis and TMSO-elimination, in accordance with the known reaction patterns of 1,3-dioxygenated dienes.[14] Methylation of **7** (Me_2SO_4/K_2CO_3) and aromatization with DDQ gave the novel 6-methoxybenzo[*c*]phenanthrene (**8**)[15] in 78% overall yield (Scheme 2).[‡] The synthesis of the functionalized [4]helicene **8** involves just five steps. Although the use of benzyne as a dienophile constitutes a straightforward route to the synthesis of helicenes, only one such example has been reported previously.[8c]

As a continuation of our synthetic plans, we tested the reactivity of diene **6** with quinones. Surprisingly, the Diels–Alder reaction of the electron-rich silyloxydiene **6** with 1,4-benzoquinone failed at rt and only when the mixture was heated under reflux in toluene during 24 h did the reaction take place and, even then, only a modest yield of 16% was obtained. These results led us to consider more electron-deficient quinones as dienophiles and we focused our attention on sulfinylquinones,[16] which have been successfully employed in Diels–Alder reactions and provide one of the few examples of the enantiopure synthesis of helicenequinones.[17,18] Interestingly, the reaction of the 1,3-silyloxydiene **6** with 2-(*p*-tolylsulfinyl)-1,4-benzoquinone[19] (**10**, 1.5 equiv.) proceeded smoothly in THF at rt to afford the dihydrobenzo[*c*]phenanthrene-1,4-quinone **11** in 62% yield (93% yield based on recovered 2-acetyl-1-tetralone) in only a few hours. In accordance with previous findings by Carreño's group,[20] the Diels–Alder reaction of sulfinylquinone **10** with an the electron-rich diene such as **6**, took place chemoselectively across the substituted sulfinyl olefin. The formation of **11** involves a domino four-step sequence: cycloaddition, sulfoxide elimination, trimethylsilyl enol ether hydrolysis and TMSO-elimination. Treatment of **11** with Me_2SO_4/K_2CO_3 and DDQ gave the 6-methoxy benzo[*c*]phenanthrene-1,4-quinone (**12**)[21] in four reaction vessels from commercial 2-acetyl-1-tetralone (Scheme 3).



Scheme 2.

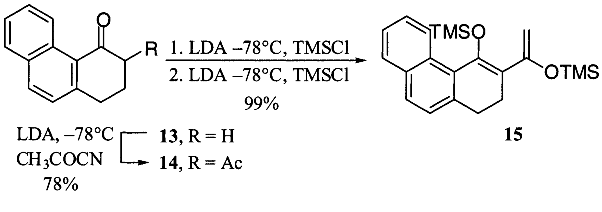


Scheme 3.

Once the Diels–Alder strategy for the preparation of helicenes using inner–outer ring 1,3-bis(trimethylsilyloxy)-1,3-dienes had been successfully validated with the synthesis of [4]helicenes, we moved forward toward the synthesis of [5]helicenes. These compounds are more strained molecules, exhibit higher racemization barriers than [4]helicenes and their synthesis constitutes a more attractive goal.[6]

For the synthesis of [5]helicenes we started with commercially available 1,2,3,4-tetrahydrophenanthren-4-one (**13**), which was acetylated by treatment with LDA and pyruvonitrile to give **14** in 78% yield. Subsequent sequential treatment of the 1,3-dicarbonyl compound **14** with LDA/TMSCl (twice) gave the novel 1,3-bis(trimethylsilyloxy)-1,3-diene **15** in quantitative yield (Scheme 4).

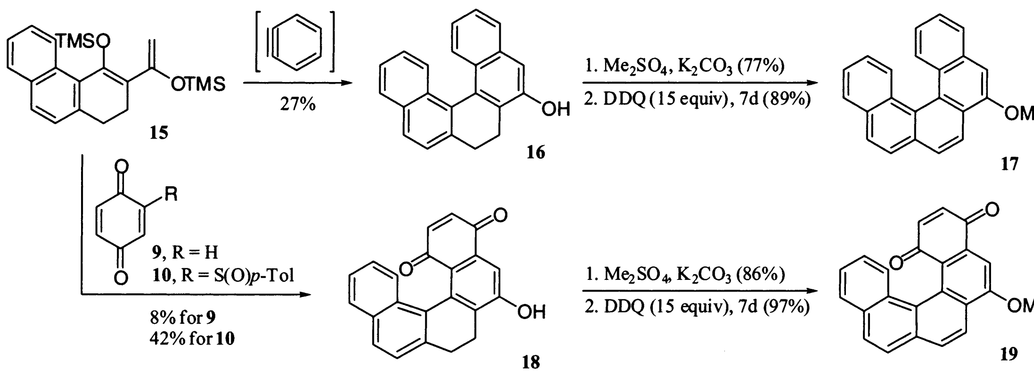
Reaction of the silyloxydiene **15** with benzyne[13] in THF at reflux afforded the dihydro[5]helicene **16** in 27% yield (44% based on recovered **14**). As found previously, significant amounts of the silyloxydiene were



Scheme 4.

[†] For a detailed experimental procedure for the preparation of this type of dienes, see Ref. 12.

[‡] All compounds described in this paper exhibit spectroscopic data completely in accordance with their assigned structures.



Scheme 5.

hydrolyzed in the reaction medium. The [5]helicene derivative **16** was fully aromatized by following the previously described two-step sequence (Scheme 5). In this way the novel 6-methoxy-[5]helicene (**17**)[22] was prepared in five steps from the commercial tetrahydrophenanthrenone **13**. At this point we also attempted the synthesis of the corresponding [5]helicenequinone by Diels–Alder reaction of diene **15** with 1,4-benzoquinone. As in the case of diene **6**, the reaction between 1,3-silyloxydiene **15** and 1,4-benzoquinone (**9**) only took place upon heating in benzene at reflux and, once again, gave only a very low yield (8%). Nevertheless, when 2-(*p*-tolylsulfinyl)-1,4-benzoquinone (**10**) was used as the dienophile, the Diels–Alder reaction with diene **15** proceeded at rt to give 42% yield (70% yield based on recovered 2-acetyl-1-tetralone) of the dihydro[5]helicenequinone **18** as the only isolated cyclization product. As discussed before, the Diels–Alder reaction of this type of electron-rich diene takes place chemoselectively across the substituted sulfinyl olefin. Treatment of dihydro[5]helicenequinone **18** with Me_2SO_4/K_2CO_3 followed by dehydrogenation with DDQ afforded the novel 6-methoxy-[5]helicene-1,4-quinone (**19**)[23] in 83% overall yield (two steps, Scheme 5).

In conclusion, functionalized [4]helicenes and [5]helicenes can be prepared by Diels–Alder reactions between inner–outer ring 1,3-bis(trimethylsilyloxy)-1,3-dienes and benzyne or quinones as dienophiles. The synthetic sequence involves just four to five steps. The use of sulfinylquinones markedly increases the Diels–Alder reactivity and could provide an interesting route for the synthesis of enantiopure helicenes.[20–22] Studies aimed at ascertaining the usefulness of this methodology for the synthesis of more complex helicenes as well as in asymmetric synthesis are now in progress.

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15. Compound **8**: Yellow oil; $R_f = 0.59$ (30% EtOAc/hexanes); ^{1}H NMR (200 MHz, CDCl$_3$): δ 4.15 (s, 3H), 7.19 (s, 1H), 7.56 (m, 2H), 7.66 (m, 2H), 7.93 (m, 2H), 8.03 (m, 1H), 8.38 (d, $J = 8.8$ Hz, 1H), 9.02 (d, $J = 7.3$ Hz, 1H), 9.13 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (50 MHz, CDCl$_3$): δ 55.7 (CH$_3$), 103.3 (CH), 120.0 (CH), 123.6 (CH), 125.1 (C), 125.9 (CH), 126.0 (CH), 126.17 (CH), 126.23 (C), 127.1 (CH), 127.3 (CH), 128.0 (CH), 128.2 (CH), 128.4 (CH), 128.7 (C), 130.0 (C), 133.6 (C), 134.1 (C), 153.5 (C); MS (EI, 70 eV) *m*/*z* (%): 259 (M$^+$+1, 19), 258 (M$^+$, 100), 215 (94); HRMS (EI) calcd for $C_{19}H_{14}O$: 258.1045, found: 258.1054.
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21. Compound **12**: Yellow solid (mp 223–225°C); $R_f = 0.60$ (40% EtOAc/hexanes); ^{1}H NMR (200 MHz, CD$_2$Cl$_2$): δ 4.16 (s, 3H), 6.89 and 7.03 (2d, AB system, $J = 10.0$ Hz, 2H), 7.43 (dt, $J = 6.8$, 1.5 Hz, 1H), 7.57 (s, 1H), 7.62 (d, $J = 6.8$ Hz, 1H), 7.89 (d, $J = 9.0$ Hz, 2H), 8.19 (d, $J = 9.0$ Hz, 1H), 8.30 (d, $J = 8.3$ Hz, 1H); ^{13}C NMR (50 MHz, CD$_2$Cl$_2$): δ 56.9 (CH$_3$), 102.0 (CH), 119.3 (CH), 125.1 (CH), 125.9 (C), 126.1 (C), 128.2 (CH), 128.3 (CH), 129.5 (C), 130.3 (CH), 130.7 (CH), 131.3 (C), 134.2 (C), 135.2 (C), 135.7 (CH), 140.9 (CH), 160.0 (C), 185.7 (C), 187.2 (C); HRMS (EI) calcd for $C_{19}H_{12}O_3$: 288.0786, found: 288.0793.
22. Compound **17**: Yellow solid (mp 204–206°C); $R_f = 0.66$ (50% EtOAc/hexanes)]; ^{1}H NMR (200 MHz, CDCl$_3$): δ 4.17 (s, 3H), 7.07–7.31 (m, 3H), 7.18 (s, 1H), 7.48 (dt, $J = 6.8$, 1.0 Hz, 2H), 7.90 (m, 5H), 8.41 (d, $J = 8.3$ Hz, 1H), 8.51 (d, $J = 8.3$ Hz, 1H); ^{13}C NMR (50 MHz, CDCl$_3$): δ 55.8 (CH$_3$), 103.1 (CH), 120.8 (CH), 122.1 (CH), 124.3 (CH), 126.1 (CH), 126.2 (CH), 126.6 (CH), 126.66 (C), 126.72 (C), 126.76 (C), 126.82 (CH), 127.0 (CH), 127.6 (CH), 127.7 (CH), 128.3 (C), 129.0 (CH), 129.3 (CH), 131.0 (C), 132.4 (C), 132.5 (C), 133.1 (C), 153.4 (C); MS (EI, 70 eV) *m*/*z* (%) 309 (M$^+$+1, 22), 308 (M$^+$, 54), 307 (M$^+$–1, 39), 278 (M$^+$–OMe, 21), 71 (100); HRMS (EI) calcd for $C_{23}H_{16}O$: 308.1201, found: 308.1202.
23. Compound **19**: Red solid (mp 253–255°C); $R_f = 0.54$ (50% EtOAc/hexanes)]; ^{1}H NMR (200 MHz, CDCl$_3$): δ 4.23 (s, 3H), 6.87 and 6.97 (2d, AB system, $J = 10.2$ Hz, 2H), 7.50 (m, 2H), 7.63 (s, 1H), 7.85 (d, $J = 8.8$ Hz, 1H), 7.98 (m, 3H), 8.37 (d, $J = 8.3$ Hz, 1H), 8.44 (d, $J = 7.3$ Hz, 1H); ^{13}C NMR (50 MHz, CDCl$_3$): δ 56.5 (CH$_3$), 100.6 (CH), 119.9 (CH), 125.7 (CH), 125.9 (CH), 126.1 (CH), 126.7 (C), 127.6 (C), 128.0 (CH), 128.1 (C), 128.2 (CH), 128.5 (C), 129.3 (CH), 129.9 (CH), 131.5 (C), 132.3 (C), 132.4 (C), 132.9 (C), 136.0 (CH), 140.0 (CH), 159.4 (C), 185.3 (C), 185.6 (C); MS (EI, 70 eV) *m*/*z* (%): 339 (M$^+$+1, 24), 338 (M$^+$, 100), 337 (M$^+$–1, 34), 323 (M$^+$–CH$_3$, 21); HRMS (EI) calcd for $C_{23}H_{14}O_3$: 338.0942, found: 338.0946.