Pergamon

*Tetrahedron Letters*, Vol. 35, No. 27, pp. 4839-4842, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)00891-4

# A New Route to Phenanthrene Derivatives

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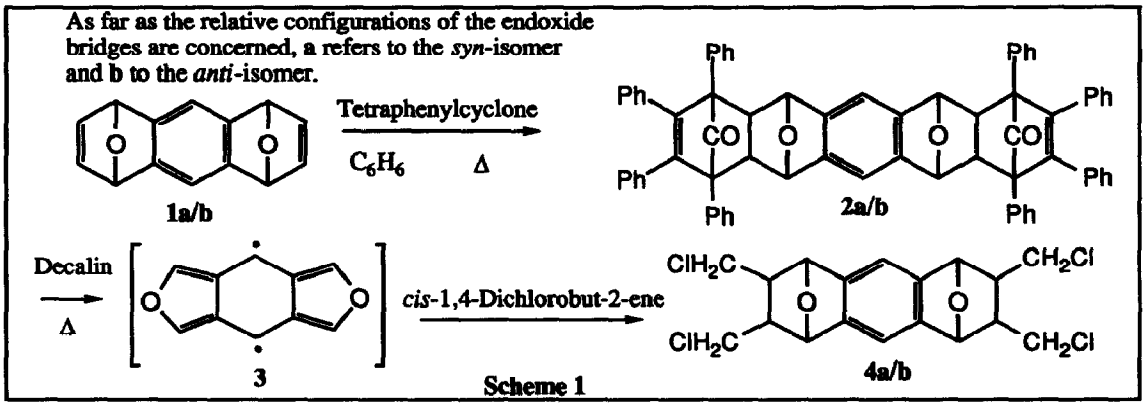
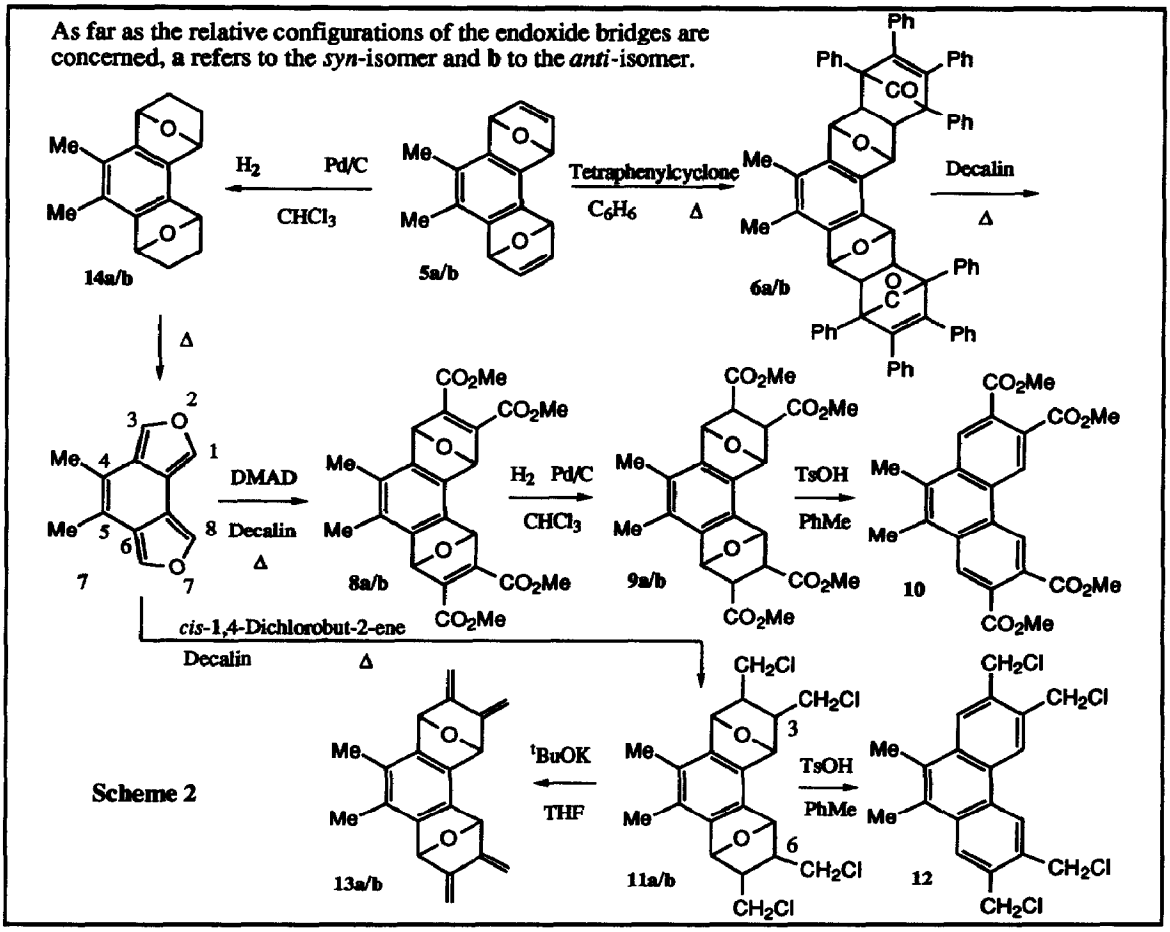
*Abstract*: 4,5-Dimethylbenzo[1,2-*c*:3,4-*c*']difuran (**7**) is a highly reactive bisdiene, which undergoes Diels-Alder reactions with a wide variety of dienophiles, including dimethyl acetylenedicarboxylate and *cis*-1,4-dichlorobut-2-ene, to give phenanthrene derivatives, *e.g.* **10** and **12**, respectively, following (hydrogenation and) dehydration of the bisadducts **8** and **11**, respectively. 9,10-Dimethyl-1,4:5,8-diepoxy-1,4,5,8-tetrahydro-phenanthrene (**5**), as a result of thermal decomposition of either (i) its bisadduct **6** with tetraphenylcyclopenta-dienone or (ii) its hydrogenated derivative **14**, is a very convenient precursor of **7**.

Benzo[c]furans have been studied extensively[1]. They are valuable precursors for the synthesis of polycyclic natural products and aromatic hydrocarbons, as a result of Diels-Alder reactions they undergo readily with various dienophiles[2]. Recently, a mixture of *syn*- and *anti*-1,4:5,8-diepoxy-1,4,5,8-tetrahydroanthracene **1a/b** has been reacted (**Scheme 1**)[3] with tetraphenylcyclopentadienone (tetraphenylcyclone) to give the linear pentacenes **2a/b**, which, upon thermal decomposition, afford benzo[1,2-*c*:4,5-*c*']difuran **3**. Trapping of **3** with dienophiles, *e.g.* 1,4-dichlorobut-2-ene, provides (**Scheme 1**) a synthetic entry into *linear* acene derivatives.




**Scheme 1**

Although the *angular* analogue of **3** – namely benzo[1,2-*c*:3,4-c']difuran (**7** in **Scheme 2** where the Me groups are replaced by H atoms) – has been reported[4], the reactivities of these compound types as bisdienes are unknown to the best of our knowledge. Moreover, little detail is available in the literature regarding their preparation. Here, we describe the synthesis, isolation, characterisation, and some Diels-Alder reactions undergone by 4,5-dimethylbenzo-[1,2-*c*:3,4-c']difuran (**7**). In the course of our investigations into the synthesis of the cyclacene derivatives, containing linearly[5] and angularly[6] fused six-membered rings by means of repetitive Diels-Alder reactions between exocyclic butadiene units (the diene) and endocyclic double bonds (the dienophile) associated with 7-oxanorbornane skeletons, we have synthesised gram-quantities of the *syn*- and (±)-*anti*-9,10-dimethyl-1,4:5,8-diepoxy-1,4,5,8-tetrahydrophenanthrenes **5a/b**. Thus, we decided to explore the possibility of using the synthetic strategy employed successfully with the *linear* difuran **3** for the preparation of the *angular* difuran **7**.




Scheme 2

When the *syn*-isomer **5a** was heated under reflux with two molar equivalents of tetraphenylcyclone in benzene[7] only *one* of the numerous possible isomeric bisadducts **6a** was isolated (**Scheme 2**). Although it was not possible to assign the relative stereochemistries to the bridging carbonyl groups in the terminal six-membered rings, the absence of a sizeable vicinal coupling constant[8] in the $^1$H NMR spectrum[7], between the endoxide bridgehead methine protons and the methine protons at the newly-formed ring junctions, indicates that these latter hydrogen atoms are oriented *endo* with respect to the 7-oxanorbornene ring systems. The presence of only *one* signal for the methyl protons and of only *four* signals for the ring junction methine protons in **6a** supports the hypothesis that both cycloadditions take place with the same relative stereochemistries at both dienophilic units in **5a**, thus maintaining the $C_s$ symmetry of the starting material. Reaction of the *anti*-isomer (±)-**5b** with tetraphenylcyclone in benzene[9] gave only *one* racemic compound (±)-**6b**. The analysis of its spectroscopic characteristics[9] supports the assignments of local relative stereochemistries, analogous to those proposed for the *syn*-isomer **6a**, but this time maintaining the $C_2$ symmetry of the starting material. Since the relative stereochemistry of the endoxide bridges is lost during the formation of **7**, the pentaphene derivatives **6a/b** were subsequently prepared and tested in the form of an isomeric mixture, as possible precursors of **7**, by heating **6a/b** in decalin under reflux in the presence of an excess of dimethyl acetylenedicarboxylate (DMAD) under an atmosphere of argon. After removal of the decalin under reduced pressure, the residue was extracted with hot MeOH. The extract was concentrated and the residue subjected to flash column chromatography ($SiO_2$:$CH_2Cl_2$/MeOH from 100/0 to 0/100) to give an

isomeric mixture (1:3) of the *syn*- and (±)-*anti*-tetraesters **8a/b** in a combined yield of 37%. To date, no attempt has been made to optimise the yield obtained in this reaction. Only the major isomer was isolated pure[10] by fractional crystallisation from $Me_2CO$. Although its relative stereochemistry has not been assigned so far, we believe that it is probably the *anti*-isomer (±)-**8b**. Pyrolysis of **6a/b** in the presence of *cis*-1,4-dichlorobut-2-ene also gave only *one* crystalline bisadduct as the major product in 37% yield. The presence of a vicinal coupling constant[8] of *ca.* 4 Hz between the endoxide bridgehead and ring junction methine protons in the $^1H$ NMR spectrum[11] indicates that the latter have the *exo* configuration, *i.e.* the *endo*-Alder rule[12] is followed. The relative stereochemistry of the endoxide bridges has not been assigned yet. However, we believe that the isolated product[11] corresponds to the *anti*-isomer (±)-**11b**. Inspection of molecular models shows that there is severe steric crowding of the *endo* oriented chloromethyl substituents at the 3- and 6-positions in the *syn*-isomer **11a**. Thus, it is destabilised relative to the *anti*-isomer **11b**. These results, which imply the intermediacy of a benzodifuran, encouraged us to pursue the isolation of **7**. Hydrogenation of **5a/b** (Pd/C in $CHCl_3$ at atmospheric pressure) gave[13] a mixture of the *syn*- and (±)-*anti*-9,10-dimethyl-1,4:5,8-diepoxy-1,2,3,4,5,6,7,8-octahydrophenanthrenes **14a/b**. These isomers were sublimed through a Pyrex tube (1.3 metres long and 1 cm internal diameter) maintained at 450-500°C at 0.01 mm Hg. Double retro Diels-Alder ethylene extrusion afforded **7** as pale yellow crystals, that formed at the cold end of the tube which was immersed in a liquid nitrogen bath. Although **7** is stable enough to be characterised[14] by conventional methods, it tends to polymerise both in the solid state and in solution by the action of light and/or heat. The tetraesters **8a/b** were hydrogenated (Pd/C in $CHCl_3$ at atmospheric pressure) to give **9a/b**[15], which was aromatised to **10**[16] by acid-catalysed dehydration[17] (*p*-TsOH/PhMe) of **9a/b**. Acid catalysed dehydration of the tetrachlorides **11a/b**, employing similar reaction conditions gave **12**[18] in 87% yield. The tetrachlorides **11a/b** were also subjected to complete dehydrochlorination (*t*-BuOK/THF) to give (±)-*anti*-9,10-dimethyl-1,4:5,8-diepoxy-1,4,5,8-tetrahydro-2,3,6,7-tetramethylidenephenanthrene (±)-**13b**[19] in 93% yield.

The results reported in this communication demonstrate that **7** is a very reactive bisdiene, capable even of reacting with very poor dienophiles. Clearly, it is an attractive precursor for the synthesis of phenanthrene derivatives that are substituted regiospecifically at the 2-, 3-, 6-, and/or 7-positions, depending on the nature of the dienophile. Interestingly, reaction of **7** with one molar equivalent of a dienophile (*e.g.* DMAD, TCE) gives only bisadducts and unreacted **7**. Therefore, the second cycloaddition involving **7** is considerably faster than that of the first. This observation is consistent with the expected high reactivity on an intermediate isobenzofuran moiety[20] – formed, in this instance, as a result of the first cycloaddition to **7**. The higher Diels-Alder reactivity of furan, compared to thiophene, is reflected in the greater reactivity[21] of **7** in relation to its sulfur analogue, without methyl substituents at the 3- and 4-positions[22].

Currently, we are exploring the synthesis of *angular* benzofurans having substituents other than methyl groups at the 3- and 4-positions since we believe that these novel reactive bisdienes can potentially find a wide range of applications in organic synthesis. Also, as readily-available chiral building blocks, enantiomerically-pure samples of **5b** and **13b** could provide a means of synthesising optically-active helical polymers[23] as a result of regioselective and stereoselective Diels-Alder oligomerisations.[24]

**Acknowledgements.** Support from CNR (Consiglio Nazionale delle Ricerche) in Italy is acknowledged.

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7. Preparation of **6a**: **5a** (25 mg, 0.10 mmol) and tetraphenylcyclone (82 mg, 0.21 mmol) were heated under reflux in benzene (3 ml) for 24 h. The white precipitate was filtered off and characterised as **6a**: (60 mg, 0.06 mmol, 56%); m.p. 190°C; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.46 (6H, s,), 3.19 (4H, s), 5.83 (2H, s), 6.01 (2H, s), 6.91-7.02 (12H, m) and 7.32-7.46 (28H, m); $^1$H NMR (300 MHz, $C_6D_6$): δ 1.99 (6H, s), 3.01 (2H, d, A part of AB system, $J_{AB}$=8 Hz), 3.03 (2H, d, B part of AB system, $J_{AB}$=8 Hz), 5.96 (2H, s), 5.98 (2H, s), 6.80-6.95 (12H, m), 7.10-7.26 (18H, m) and 7.65-7.71 (10H, m); $^{13}$C NMR (75.46 MHz, $CDCl_3$): δ 16.2, 46.6, 46.7, 63.8, 64.6, 79.9, 80.4, 126.3-145.0 (aromatic and olefinic) and 196.6; EIMS *m/z* (rel.int.): 382(100), 186(18), 78(10).
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9. Preparation of (±)-**6b**: (±)-**5b** (500 mg, 2.10 mmol) and tetraphenylcyclone (1.620 g, 4.12 mmol) were heated under reflux in benzene (50 ml) for 20 h. The white precipitate was filtered off and characterised as (±)-**6b**: (1.900 g, 1.89 mmol, 90%); m.p. 218°C; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.48 (6H, s), 3.06 (2H, d, A part of AB system, $J_{AB}$=8Hz), 3.19 (2H, d, B part of AB system, $J_{AB}$=8 Hz), 5.86 (2H, s), 5.91 (2H, s,), 6.91-7.05 (22H, m) and 7.27-7.48 (18H, m); (±)-**6b** is considerably less soluble in most organic solvents than its isomer **6a**, thus a $^{13}$C NMR spectrum was not recorded; EIMS *m/z* (rel.int.): 382(100), 186(18), 28(5).
10. The racemic mixture (±)-**8b** could be separated from the crude product containing also the minor isomer **8a** by fractional crystallisation from acetone: m.p. 224°C; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.26 (6H, s), 3.81 (6H, s), 3.83 (6H, s), 6.01 (2H, d, A part of AB system, $J_{AB}$=1Hz) and 6.02 (2H, d, B part of AB system, $J_{AB}$=1 Hz), $^{13}$C NMR (75.46 MHz, $CDCl_3$): δ 15.4, 52.4, 52.5, 83.5, 83.8, 129.2, 135.5, 141.4, 149.7, 150.4, 162.6 and 162.7; EIMS *m/z* (rel.int.): 470($M^+$, 20), 410(80), 350(40), 328(50), 267(100), 186(60), 171(10).
11. (±)-**11b**: m.p. 280°C (dec.) from $CHCl_3$; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.33 (6H, s), 2.58-2.69 (4H, m), 3.00-3.08 (4H, m), 5.59 (2H, d, J=4 Hz) and 5.74 (2H, d, J=4 Hz); $^{13}$C NMR (75.46 MHz, $CDCl_3$): δ 16.3, 41.9, 42.6, 44.4, 45.5, 81.3, 81.7, 130.0, 133.0 and 140.8; EIMS *m/z* (rel.int.): 436($M^+$, 10), 399(38), 310(40), 275(25), 239(5), 186(100), 128(5). No other isomeric pure adduct could be isolated from the crude reaction mixture.
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13. The crude product obtained from the hydrogenation of **5a/b** was characterised as the mixture **14a/b** on the basis of its $^1$H NMR spectrum (300 MHz, $CDCl_3$): δ 1.21-1.48 (4H, m), 1.97-2.10 (4H, m), 2.19 (3H, s), 2.21 (3H, s), 5.38-5.48 (4H, m). The hydrogenation of a pure sample of (±)-**5b** gave (±)-**14b**: m.p. 177°C from $CHCl_3$; $^1$H NMR (300 MHz, $CDCl_3$): δ 1.28-1.46 (4H, m), 1.97-2.10 (4H, m), 2.21 (6H, s), 5.41 (2H, d, J=4 Hz) and 5.46 (2H, d, J=4 Hz); $^{13}$C NMR (75.46 MHz, $CDCl_3$): δ 15.3, 26.2, 26.8, 77.7, 77.9, 125.4, 133.0 and 143.1; EIMS *m/z* (rel.int.): 242 ($M^+$, 15), 214(45), 186(100).
14. **7**: m.p. 150°C.; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.1 (6H, s), 7.63 (2H, d, J=1.5 Hz) and 7.82 (2H, d, J=1.5 Hz); $^{13}$C NMR (75.46 MHz, $CDCl_3$): δ 14.5, 113.4, 120.7, 125.5, 135.7, 135.9; EIMS *m/z* (rel.int.): 186($M^+$, 100), 171(58), 157(6).
15. The crude product obtained from the hydrogenation of **8a/b** was characterised as the mixture **9a/b** on the basis of its $^1$H NMR spectrum (300 MHz, $CDCl_3$): δ 2.22 (6H, s), 2.28 (6H, s), 3.45 (3H, s), 3.49 (3H, s), 3.52 (3H, s), 3.53 (3H, 3s), 3.65-3.74 (4H, m) and 5.53-5.62 (4H, m). The hydrogenation of a pure sample of (±)-**8b** gave (±)-**9b**: m.p. 215°C; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.22 (6H, s), 3.49 (6H, s), 3.53 (6H, s), 3.66 (2H, A part of 2 x ABMX systems, $J_{AB}$=10.5 Hz, $J_{AX}$=4.5 Hz, $J_{AM}$=0.0 Hz), 3.67 (2H, B part of 2 x ABMX systems, $J_{AB}$=10.5 Hz, $J_{BM}$=4.5 Hz, $J_{BX}$=0.0 Hz), 5.59 (4H, M part of 2 x ABMX systems, $J_{BM}$=4.5 Hz, $J_{AM}$=0.0 Hz, $J_{MX}$=0.0 Hz) and 5.62 (4H, X part of 2 x ABMX systems, $J_{AX}$=4.5 Hz, $J_{BX}$=0.0 Hz, $J_{MX}$=0.0 Hz); $^{13}$C NMR (75.46 MHz, $CDCl_3$): δ 15.8, 47.7, 47.8, 51.6, 51.7, 79.9, 80.1, 128.7, 133.2, 140.9, 169.9 and 170.8; EIMS *m/z* (rel.int.): 474($M^+$, 1), 443(6), 330(43), 186(100), 171(6), 113(13).
16. **10**: $^1$H NMR (300 MHz, $CDCl_3$): δ 2.79 (6H, s), 4.00 (6H, s), 4.02 (6H, s), 8.44 (1H, s) and 9.11 (1H, s).
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18. **12**: m.p. 220-222°C from acetone; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.73 (6H, s), 5.01 (4H, s), 5.05 (4H, s), 8.13 (2H, s) and 8.67 (2H, s); $^{13}$C NMR: δ 16.1, 44.0, 44.1, 125.6, 127.4, 129.0, 130.5, 132.8, 133.3 and 134.6; EIMS *m/z* (rel.int.): 398($M^+$, 75), 363(62), 328(10), 293(27).
19. (±)-**13b**: m.p. 255°C (dec.) from benzene; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.25 (6H, s), 5.16 (2H, s), 5.23 (2H, s), 5.26 (2H, s), 5.30 (2H, s), 5.59 (2H, s) and 5.62 (2H, s); $^{13}$C NMR (75.46 MHz, $CDCl_3$): δ 15.5, 82.4, 82.7, 102.6, 103.2, 127.6, 132.6, 142.4, 144.0 and 144.2; EIMS *m/z* (rel.int.): 290($M^+$, 100), 261(40), 233(40), 209(45).
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(*Received in UK* 30 *March* 1994; *revised* 29 *April* 1994; *accepted* 6 *May* 1994)