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TETRAHEDRON
LETTERS

[5]Helicenes by iterative radical cyclisations to arenes

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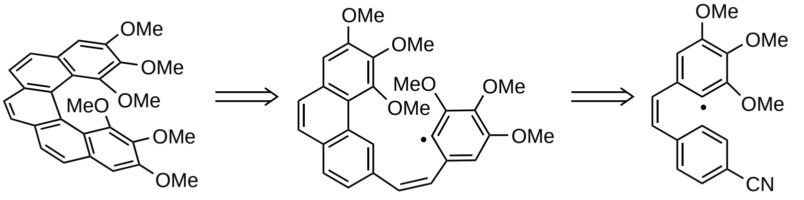
Abstract—The paper describes a synthesis of 1,2,3,12,13,14-hexamethoxy[5]helicene **1**. The synthesis features two sp^2–sp^2 bond forming reactions, each involving a 6-*exo*/*endo*-trig cyclisation of an aryl radical intermediate to an arene. © 2002 Elsevier Science Ltd. All rights reserved.

Intramolecular radical additions to arenes have acquired greater prominence in recent years as their value in synthesis has become more widely appreciated.[1,2] Our main contribution has been to show that 6-*exo*/*endo*-trig radical cyclisations to pyridines, quinolines and arenes are often facile and high yielding processes.[3–5] One extension of the method we were keen to explore involved its application in an iterative sense for the preparation of [5]helicenes (Scheme 1). Herein we report our realisation of that objective through a short synthesis of 1,2,3,12,13,14-hexamethoxy[5]helicene **1**.

The synthesis began with the union of **5** and **7** using a standard Wittig olefination procedure. Pleasingly this gave rise to an easily separable 13:2 mixture of *cis*- and *trans*-stilbenes **8** in 97% yield. Treatment of *cis*-**8** with tributyltin hydride under standard radical forming conditions then provided phenanthrene **9** in 85% yield.[5] A series of functional group interconversions next transformed the nitrile function into a phosphonium salt, facilitating the preparation of stilbene **14** by a Wittig olefination with **5**. This too proved to be selective for the desired *cis*-stilbene **14** (48% yield), and again column chromatography readily effected its separation from *trans*-**14** (19%). To complete the synthesis of [5]helicene **1**, *cis*-stilbene **14** was exposed to tributyltin hydride under standard radical forming conditions.[5] This gave 1,2,3,12,13,14-hexamethoxy[5]helicene **1** and 1,2,3,8,9,10-hexamethoxydibenzo[*a*,*h*]anthracene **15** in 52% and 17% yields, respectively (Scheme 2).

The clear preference for cyclisation of radical intermediate **2** to C-5 of the phenanthrene moiety rather than C-7 is notable (Scheme 3). Though the origin of that selectivity has yet to be established with rigor, we presume it reflects a more favourable SOMO–LUMO interaction with C-5. The formation of **1** as the major product additionally suggests that cyclisation to **16** or **17** and the subsequent loss of a hydrogen atom are irreversible: the lack of products derived from migration of the alkene tether lending further support to this hypothesis.

In conclusion, we have developed a new approach to [5]helicenes in which two sp^2–sp^2 coupling reactions are



Scheme 1.

Keywords: helicenes; radicals and radical reactions; cyclisation; polycyclic aromatic compounds.

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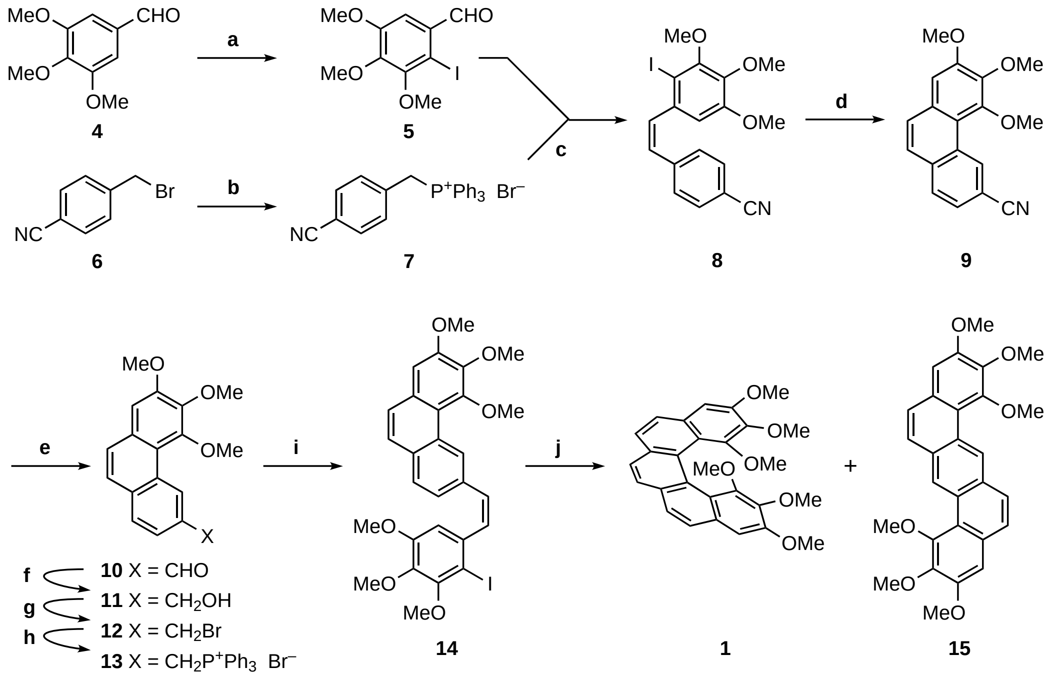
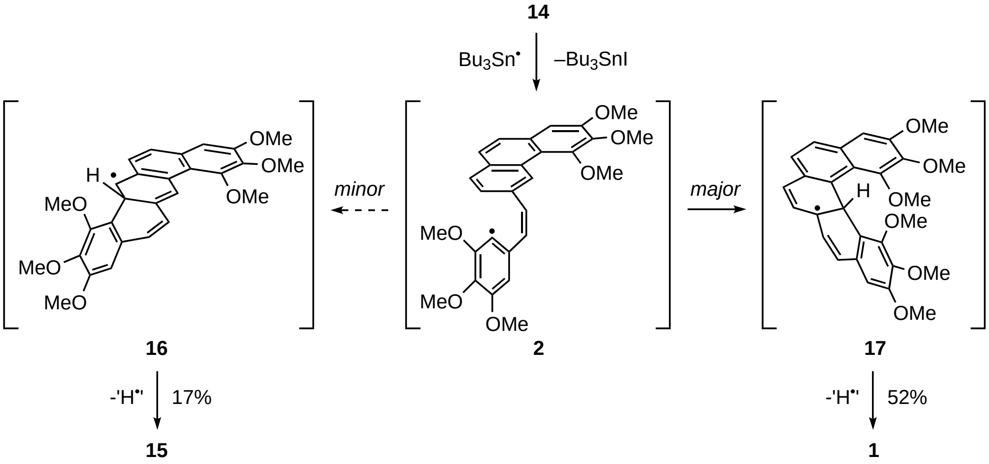


Scheme 2. *Reagents and conditions*: **a**. I_2, $AgCO_2CF_3$, DCM, 7 h, rt, 92%;[6] **b**. PPh_3, PhMe, reflux, 6 h, 96%;[7] **c**. NaH, THF, 0°C→rt, 2 h; add **5** at 0°C→rt, 2 h, 97% (*Z*:*E*–13:2); **d**. Bu_3SnH, AIBN, PhMe, 90°C, 36 h; $KF_{(aq)}$, rt, 16 h, 85%;[5] **e**. DIBAL-H, PhMe, 0°C, 1 h, 81%;[8] **f**. $NaBH_4$, THF, rt, 4 h, 96%; **g**. PBr_3, PhH, rt, 2 h, 85%; **h**. PPh_3, PhMe, reflux, 6 h, 70%; **i**. NaH, THF, 0°C→rt, 2 h; add **5** at 0°C→rt, 16 h, 67% (*Z*:*E*–5:2); **j**. Bu_3SnH, AIBN, PhMe, 90°C, 16 h; $KF_{(aq)}$, rt, 16 h, 69% (**1**:**15**–3:1).[5]



Scheme 3.

accomplished by 6-*exo*/*endo*-trig cyclisation of an aryl radical to an arene.[5] The synthesis demonstrates the potential of this method in the construction of strained polyaromatics and has led to a greater understanding of the mechanistic course of this recently uncovered reaction.

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References

1. For recent examples of radical additions to arenes see: (a) Clive, D. L. J.; Kang, S. *J. Org. Chem.* **2001**, *66*, 6083; (b) Leardini, R.; McNab, H.; Minozzi, M.; Nanni, D. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1072; (c) Harrowven, D. C.; Nunn, M. I. T.; Newman, N. A.; Fenwick, D. R. *Tetrahedron Lett.* **2001**, *42*, 961; (d) Ishibashi, H.; Kobayashi, T.; Nakashima, S.; Tamura, O. *J. Org. Chem.* **2000**, *65*, 9022; (e) Senboku, H.; Hasegawa, H.; Orito, K.; Tokuda, M. *Tetrahedron Lett.* **2000**, *41*, 5699; (f) Amrein, S.; Bossart, M.; Vasella, T.; Studer, A. *J. Org. Chem.* **2000**, *65*, 4281; (g) Bowman, W. R.; Mann, E.; Parr, J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2991; (h) Wakabayashi, K.;

Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Org. Lett.* **2000**, *2*, 1899; (i) Clive, D. L. J.; Kang, S. *Tetrahedron Lett.* **2000**, *41*, 1315; (j) Studer, A.; Bossart, M.; Vasella, T. *Org. Lett.* **2000**, *2*, 985; (k) Ishibashi, H.; Ohata, K.; Niihara, M.; Sato, T.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **2000**, 547; (l) Bonfand, E.; Forslund, L.; Motherwell, W. B.; Vázquez, S. *Synlett* **2000**, 475; (m) Motherwell, W. B.; Vázquez, S. *Tetrahedron Lett.* **2000**, *41*, 9667; (n) Wang, S.-F.; Chuang, C.-P.; Lee, J. H.; Liu, S.-T. *Tetrahedron* **1999**, *55*, 2273; (o) Ishibashi, H.; Toyao, A.; Takeda, Y. *Synlett* **1999**, 1468; (p) Ishibashi, H.; Kobayashi, T.; Takamasu, D. *Synlett*, **1999**, 1286; (q) Studer, A.; Bossart, M.; Steen, H. *Tetrahedron Lett.* **1998**, *39*, 8829; (r) Aicaide, B.; Rodríguez-Vincente, A. *Tetrahedron Lett.* **1998**, *39*, 6589; (s) Studer, A.; Bossart, M. *Chem. Commun.* **1998**, 2127; (t) Amii, H.; Kondo, S.; Uneyama, K. *Chem. Commun.* **1998**, 1845; (u) Godfrey, C. R. A.; Hegarty, P.; Motherwell, W. B.; Uddin, M. K. *Tetrahedron Lett.* **1998**, *39*, 723; (v) Giraud, L.; Lacôte, E.; Renaud, P. *Helv. Chim. Acta* **1997**, *80*, 2148; (w) Rosa, A. M.; Lobo, A. M.; Branco, P. S.; Prabhakar, S. *Tetrahedron* **1997**, *53*, 285; (x) Bonfand, E.; Motherwell, W. B.; Pennell, A. M. K.; Uddin, M. K.; Ujjainwalla, F. *Heterocycles* **1997**, *46*, 523; (y) da Mata, M. L. E. N.; Motherwell, W. B.; Ujjainwalla, F. *Tetrahedron Lett.* **1997**, *38*, 141; (z) da Mata, M. L. E. N.; Motherwell, W. B.; Ujjainwalla, F. *Tetrahedron Lett.* **1997**, *38*, 137.

2. For a recent overview see: Studer, A.; Bossart, M. *Tetrahedron* **2001**, *57*, 9649.
3. (a) Harrowven, D. C.; Sutton, B. J.; Coulton, S. *Tetrahedron Lett.* **2001**, *42*, 9061; (b) Harrowven, D. C.; Nunn, M. I. T.; Blumire, N. J.; Fenwick, D. R. *Tetrahedron* **2001**, *57*, 4447; (c) Harrowven, D. C.; Nunn, M. I. T.; Blumire, N. J.; Fenwick, D. R. *Tetrahedron Lett.* **2000**, *41*, 6681; (d) Harrowven, D. C.; Nunn, M. I. T. *Tetrahedron Lett.* **1998**, *39*, 5875.
4. (a) Harrowven, D. C.; Sutton, B. J.; Coulton, S. *Tetrahedron* **2002**, *58*, in press; (b) Harrowven, D. C.; Sutton, B. J.; Coulton, S. *Tetrahedron Lett.* **2001**, *42*, 2907.
5. (a) Harrowven, D. C.; Nunn, M. I. T.; Fenwick, D. R. *Tetrahedron Lett.* **2002**, *43*, 3185; (b) Aidhen, I. S.; Narasimhan, N. S. *Indian J. Chem. Sect. B* **1993**, *32*, 211.
6. Bradley, A.; Motherwell, W. B.; Ujjainwalla, F. *Chem. Commun.* **1999**, *10*, 917.
7. Rafizadeh, K.; Yates, K. *J. Org. Chem.* **1984**, *49*, 1500.
8. Wen, L.; Li, M.; Schlenoff, J. B. *J. Am. Chem. Soc.* **1997**, *119*, 7726.