Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters 47 (2006) 2299–2304
Tetrahedron Letters

A formal synthesis of aflatoxin B2: a Dötz benzannulation approach

Stephen A. Eastham,[a] Steven P. Ingham,[a] Michael R. Hallett,[a] John Herbert,[b] Peter Quayle[a,*] and James Raftery[a]

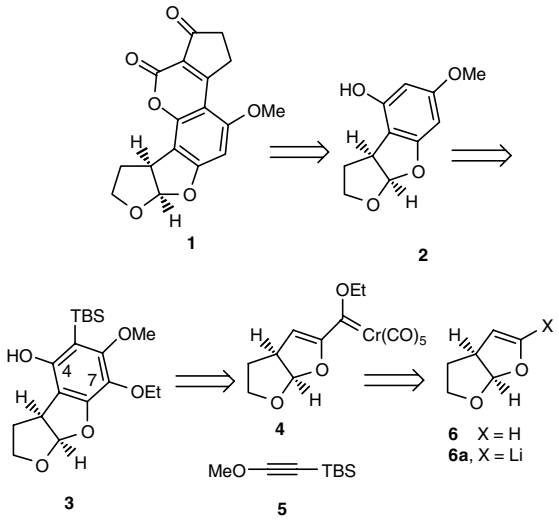
[a]*School of Chemistry, The University of Manchester, Manchester M13 9PL, UK*
[b]*Sanofi-Synthélabo, Willowburn Avenue, Alnwick, Northumberland NE66 2JH, UK*

Received 5 January 2006; revised 2 February 2006; accepted 3 February 2006
Available online 21 February 2006

Abstract—A Dötz benzannulation reaction has been utilized in the synthesis of the furo[2,3-*b*]furan core of aflatoxin B2.

Since its discovery in 1975, the Dötz benzannulation reaction[1] has enjoyed considerable attention from the synthetic community as it enables the regiocontrolled preparation of aromatic systems from acyclic precursors. Our interest[2] in this area lies in the application of the Dötz reaction to the synthesis of benzofuran and benzopyran ring systems present in a variety of natural products and necessitates the use of heterofunctionalized Fischer carbene complexes in the key benzannulation step. There are relatively few methodological studies[2,3] concerning the use of Fischer carbene complexes possessing this basic skeleton, and to our knowledge, no applications of furo[2,3-*b*]furanyl derived Fischer carbene complexes in natural product synthesis.

In this letter we present our findings on the application of the Dötz reaction to the synthesis of aflatoxin B2, **1**, a representative member of the furo[2,3-*b*]benzofuran family of mycotoxins (Scheme 1). Our initial target lay in the synthesis of racemic **2**, an intermediate, which has been commonly promulgated[4] as a synthetic precursor to the natural product. We surmised that **2** would be accessible from the Dötz reaction between the furo[2.3-*b*]-furan-2-yl carbene complex **4** and the functionalized alkyne **5**.[5] Regiochemical issues[6] arising from the use of unsymmetrical acetylenes in the Dötz reaction have been addressed by a number of workers and, although the use of oxygenated acetylenes[7] such as **5** have received scant attention in such reactions we were confident[2b,c] that the paradigm enunciated by Dötz, Yamashita and Wulff would result in the formation of the aromatic ring with the correct positioning of the methoxy substituent at C6 in **3**. What was not so clear at the outset was the manner in which the two phenolic oxygens at C4 and C7 could be differentiated in order to permit selective deoxygenation[8] at C7.



1 2 3 4 5 6 X = H 6a, X = Li

Scheme 1. Aflatoxin B2 retrosynthetic analysis.

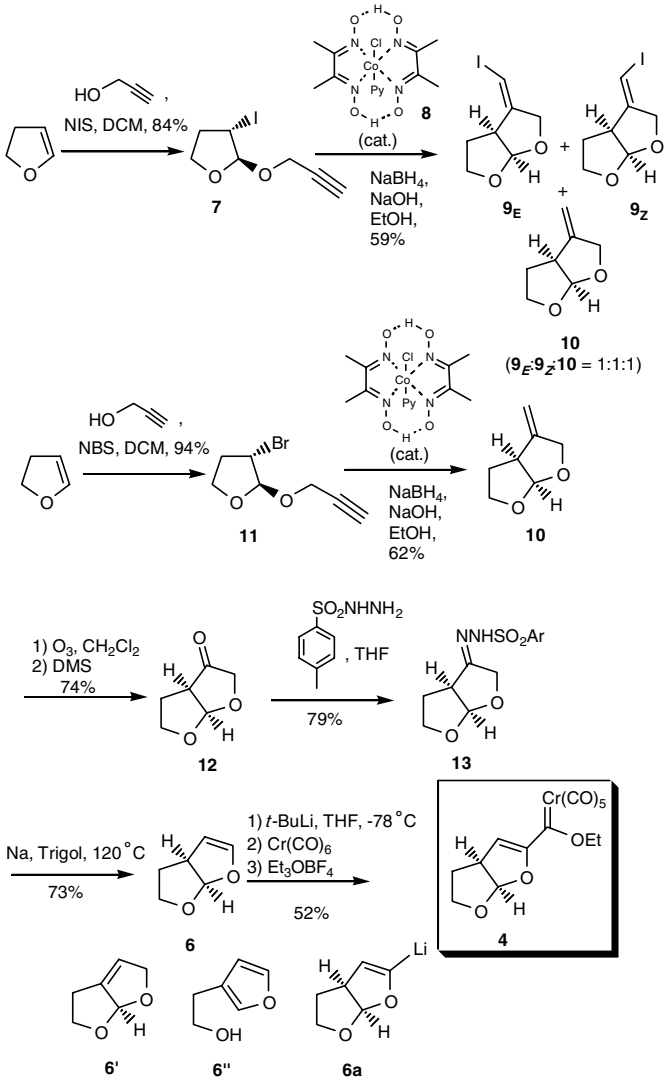
We considered that the carbene complex **4** would be accessible from the furo[2,3-*b*]furan **12**[9] using the standard Fischer procedure.[10] This necessarily entailed generation of the vinyl carbanion **6a** using Boeckman's[11] procedure, which, in this instance, was itself not assured of success. In the event enol ether **6** was prepared in a

Keywords: Dötz; Benzannulation; Carbene; Aflatoxin; Chromium.
* Corresponding author. Tel.: +44 161 275 4619; fax: +44 161 275 4598; e-mail: peter.quayle@manchester.ac.uk

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.02.024

five-step sequence from dihydrofuran as outlined in Scheme 2.

Haloetherification[12] of dihydrofuran with propargyl alcohol in the presence of NIS or NBS afforded the *trans*-haloethers **7** and **11** in near quantitative yield. Unexpectedly, and in contrast to Ghosh's[13] report, we found that cyclization (Bu_3SnH, AIBN, PhH) of the iodide **7** proved problematical as variable quantities (up to 40% isolated yield) of the vinyl iodides $\mathbf{9}_{E,Z}$ were also generated via a competing atom transfer cyclization reaction.[14] Removal of the iodide $\mathbf{9}_{E,Z}$ from the bulk sample proved impossible by chromatography or distillation. Fortunately, radical cyclization of **11** was well behaved and was best carried out using Okabe's[15] procedure, which is catalytic in **8**, and afforded the exocyclic alkene[9c,13] **10** in reproducible yields of ca. 62% on a 260 mmol scale (Scheme 2). It should be pointed out that whilst tin methodology was also effective in promoting this cyclization reaction, purification on a preparative scale became impossible due to the presence of large quantities of tin residues produced during the reaction. Ozonolysis of **10** (O_3, CH_2Cl_2, −78 °C) followed by reductive work-up (Me_2S) was routinely carried out on a 100 mmol scale and afforded the ketone **12**,[12] a low melting solid, in 74% isolated yield. Conversion of **12** to the hydrazone $\mathbf{13}_{E,Z}$ (as a 1:1 mixture of geometrical isomers) and hence to the enol ether **6** was next investigated. After careful optimization it was found that the Bamford–Stevens reaction[16,17] was best carried out by mild thermolysis of the sodium salt of **13** in trigol at 120 °C under reduced pressure (20 mmHg). Under these conditions the volatile nature of the ether **6** meant that it simply distilled out of the reaction mixture as it was formed and could be collected in a cardice trap. This procedure routinely afforded the enol ether **6** in an essentially pure state and devoid of any trace of the alternate double bond isomer **6′** or furan **6″** in >70% yield on a preparative scale. With the enol ether **6** in hand its conversion to the Fischer carbene complex **4** was pursued. In the event, our concerns over the metallation of **6** were misplaced as its exposure to *t*-Buli (1.1 equiv, THF, −78 °C, 15 min and then at 20 °C for 30 min), generating **6a**, followed by the



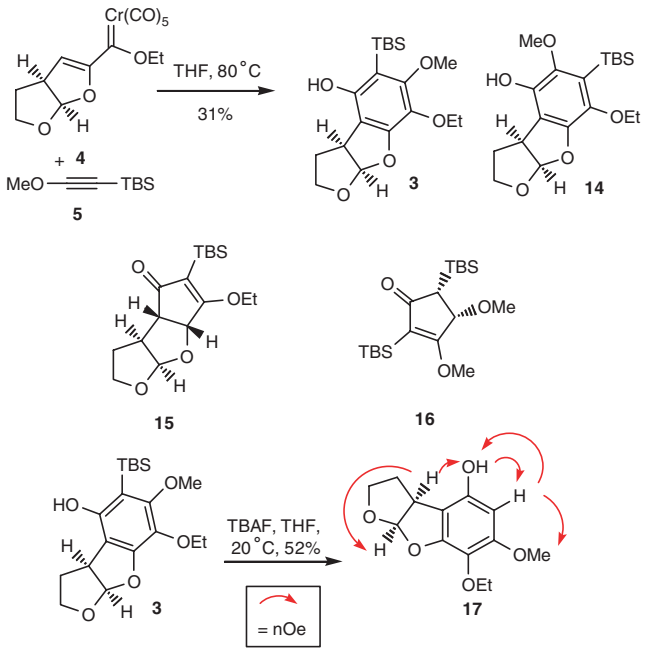
Scheme 2. Synthesis of complex **4**.

sequential addition of $Cr(CO)_6$ and Meerwein's reagent afforded the carbene complex **4**, a deep red solid, in 52% isolated yield after chromatography and recrystallization. Having developed a robust route to the carbene complex **4** its reactivity in the crucial Dötz benzannulation reaction was next addressed. Gratifyingly, exposure of the complex **4** to the acetylene **5**[5] (2.5 equiv) in THF at 80 °C for 2 h resulted in the complete consumption of the complex **4** and afforded the phenol **3** in 31% yield after column chromatography.

The observed regiochemical outcome of this reaction is in keeping with previous methodological studies[2c] and was substantiated by NOE difference measurements performed upon the desilylated phenol **17** (Scheme 3) and by subsequent chemical transformations. We were unable to detect any of the alternate regioisomeric phenol **14** in the crude reaction mixture of this Dötz reaction but were able to isolate the variable quantities of the cyclopentenones **15** (ca. 2%) and **16**[18] (<1%) whose structure was unambiguously assigned by X-ray crystallography (Fig. 1).

The product distribution of this reaction was found to be quite sensitive to the reaction conditions employed (solvent polarity, temperature and additives) but fortuitously those used in the first attempt proved to be optimal and reproducible in terms of phenol **3**.

At this stage a strategy was required, which would enable the selective deoxygenation of **3** at C7 (Scheme 4). This was readily accomplished in a three-step sequence involving oxidation of the phenol **3** to the quinone **18** (CAN, CH_3CN/H_2O), reduction to the hydroquinone **19** (H_2–Pd/C) and finally regioselective migration of the silicon substituent at C5 of **19** to the phenolic group at C4 of **20**. This 1,3-silatropic migration



Scheme 3. Dötz benzannulation sequence.

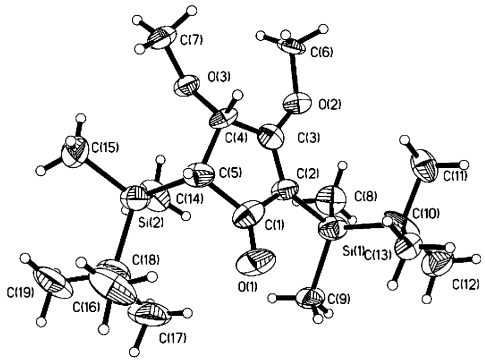
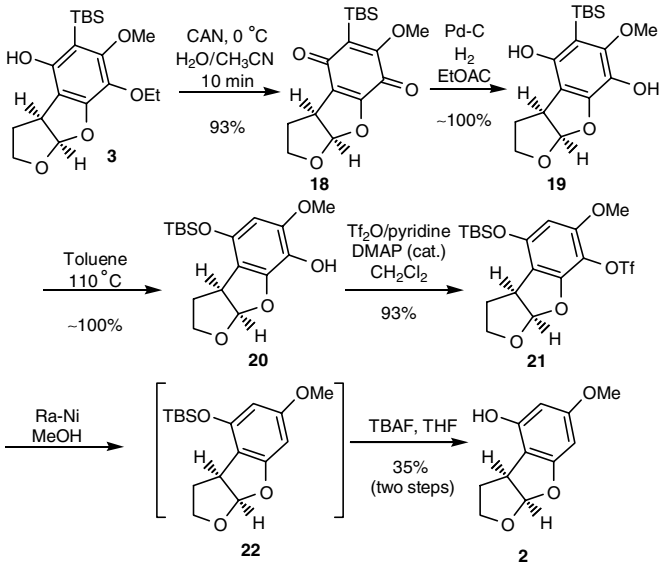


Figure 1. X-ray structure of cyclopentenone **16**.

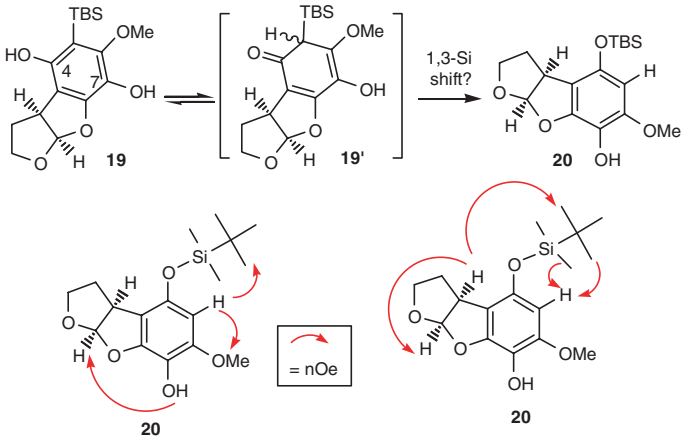
deserves some comment as it occurs essentially quantitatively upon mild thermolysis in toluene (110 °C, 1 h) and is apparently wholly regioselective. The overall yield for this sequence was pleasingly high (93%) and regiochemical issues were again addressed using NOE difference measurements (Scheme 5). Whilst there have been sporadic reports of similar silicon migrations in Dötz benzannulation reactions[19] its application to the in situ, regioselective, protection of hydroquinones (as opposed to monoalkyl derivatives[19]) has not to our knowledge been previously reported. We note[20] that mechanistic studies on related regioselective silatropic C to O migrations of polysilylated phenols are indicative of an intramolecular rearrangement although, again, such reactions have not been exploited synthetically. Presumably the rearrangement described here proceeds via the intermediacy of the tautomeric cyclohexadienone **19′**, followed by a formal 1,3-silatropic shift, the driving force for the reaction being the formation of a strong O–Si bond.[20]

With protected hydroquinone **20** in hand its deoxygenation at C7 was next attempted. Conversion of the phenol **20** to the triflate **21** was uneventful, however, its deoxygenation was more problematical. Although subjecting **21** to Sáa's[21] modification of Cacchi's conditions[22] ($PdCl_2$, dppp, HCO_2H, Bu_3N, DMF, 80 °C) did in fact effect deoxygenation with concomitant in situ deprotection to the desired intermediate **2**, the product was contaminated with *N*,*N*-dibutylformamide, which could only be removed by recrystallization resulting in a low overall isolated yield of pure material (11%). However, exposure of **21** to Raney nickel, as described by Noland,[4b] followed by desilylation (TBAF, THF, 20 °C) of the intermediate silylether **22** afforded the desired phenol **2** in 35% isolated yield over the two steps. The phenol **2** prepared in this manner was identical[23] to that described by Rapoport[4c] and Noland[4b] and therefore constitutes a formal synthesis of the natural product.

In conclusion, we have demonstrated that the Dötz reaction between a furo[2,3-*b*]furanyl carbene complex and a silylated acetylene provides ready access to a pivotal intermediate for the synthesis of aflatoxin B2. The silicon substituent fulfils two roles by controlling the regiochemistry of the initial Dötz reaction and providing a



Scheme 4. Deoxygenation at C7.



Scheme 5. Rearrangement of **19** into **20**: structural assignment.

facile means by which the selective protection–deoxygenation of a hydroquinone intermediate can be achieved. In addition, the well-behaved lithiation of the 2,3,3a,6a-tetrahydrofuro[2,3-*b*]furan nucleus demonstrates that this route could be of use in the synthesis of other furo[2,3-*b*]furan-containing organometallics and may find application in the synthesis of other natural products containing this motif.[24] Although this sequence provides access to **2** in racemic form, the ready availability[17c] of homochiral furo[2,3-*b*]furans should mean that access to optically pure intermediates using the chemistry described herein will be possible.

Acknowledgements

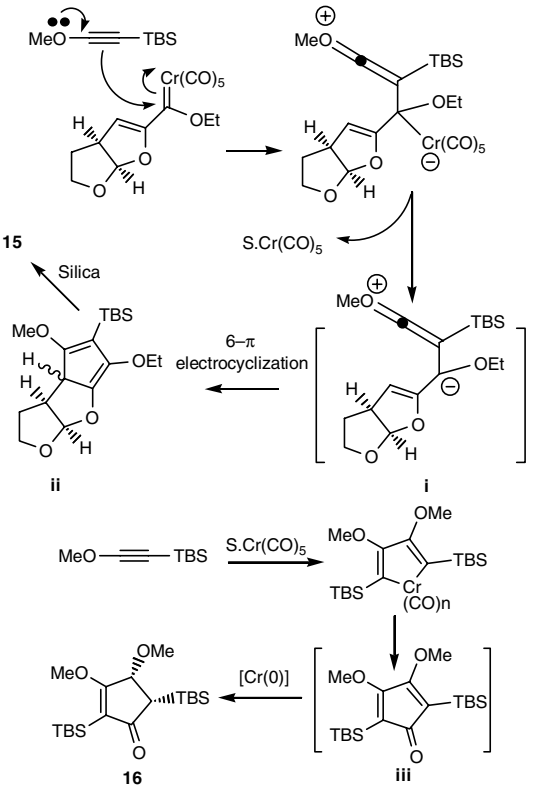
We thank Sanofi-Synthélabo (S.A.E.) for the provision of a CASE award and the EPSRC (S.P.I. and M.R.H.) for postgraduate studentships (GR/K/16197).

References and notes

1. Dötz, K. H. *Angew. Chem.* **1975**, *87*, 672; For reviews see: Dötz, K. H.; Tomuschat, P. *Chem. Soc. Rev.* **1999**, *28*, 187; de Meijere, A.; Schirmer, H.; Duetsch, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 3964; Dötz, K. H.; Stendel, J. In *Modern Arene Chemistry*; Astruc, D., Ed.; Wiley-VCH: Weinheim, Germany, 2002; For recent applications see: Shanmugasundaram, M.; Garcia-Martinez, I.; Li, Q.; Estrada, A.; Martinez, N. E.; Martinez, L. E. *Tetrahedron Lett.* **2005**, *46*, 7545; Gupta, A.; Sen, S.; Harmata, M.; Pulley, S. R. *J. Org. Chem.* **2005**, *70*, 7422; Pulley, S. R.; Czako, B. *Tetrahedron Lett.* **2004**, *45*, 5511; Roush, W. R.; Neitz, R. J. *J. Org. Chem.* **2004**, *69*, 4906; Vorogushin, A. V.; Wulff, W. D.; Hansen, H.-J. *J. Org. Chem.* **2003**, *68*, 9618.
2. (a) Hallett, M. R.; Painter, J. E.; Quayle, P.; Ricketts, D. *Tetrahedron Lett.* **1998**, *39*, 2851; (b) Beddoes, R. L.; Painter, J. E.; Quayle, P.; Patel, P. *Tetrahedron* **1997**, *53*, 17297; (c) Beddoes, R. L.; Painter, J. E.; Quayle, P.; Patel, P. *Tetrahedron Lett.* **1996**, *37*, 9385; (d) Painter, J. E.;

Quayle, P.; Patel, P. *Tetrahedron Lett.* **1995**, *36*, 8089; (e) Beddoes, R. L.; King, J. D.; Quayle, P. *Tetrahedron Lett.* **1995**, *36*, 3027; (f) King, J. D.; Quayle, P. *Tetrahedron Lett.* **1991**, *32*, 7759; (g) King, J.; Quayle, P.; Malone, J. F. *Tetrahedron Lett.* **1990**, *31*, 5221; (h) Eastham, S. A.; Herbert, J.; Painter, J. E.; Patel, P.; Quayle, P. *Synlett* **1998**, 61.

3. White, J. D.; Smits, H. *Org. Lett.* **2005**, *7*, 235; Barluenga, J.; Vicente, R.; López, L. A.; Rubio, E.; Tomás, M. *J. Am. Chem. Soc.* **2004**, *126*, 5975; Barluenga, J.; Vicente, R.; López, L. A.; Rubio, E.; Tomás, M.; Álvarez-Rúa, C. *J. Am. Chem. Soc.* **2004**, *126*, 470; Barluenga, J.; Aznar, F.; Gutiérrez, I.; Martin, J. A. *Org. Lett.* **2002**, *4*, 2719; Dötz, K. H.; Otto, F.; Nieger, M. *J. Organomet. Chem.* **2001**, *621*, 77; Waters, M. L.; Brandvold, T. A.; Isaacs, L.; Wulff, W. D.; Rheingold, A. L. *Organometallics* **1998**, *17*, 4298; Chan, K. S.; Zhang, H. *Synth. Commun.* **1995**, *25*, 635; Harvey, D. F.; Grenzer, E. M.; Gantzel, P. K. *J. Am. Chem. Soc.* **1994**, *116*, 6719; Wulff, W. D.; Bax, B. M.; Brandvold, T. A.; Chan, K. S.; Gilbert, A. M.; Hsung, R. P.; Mitchell, J.; Clardy, J. *Organometallics* **1994**, *13*, 102; Brandvold, T. A.; Wulff, W. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1990**, *112*, 1645; Chan, K. S.; Peterson, G. A.; Brandvold, T. A.; Faron, K. L.; Challener, C. A.; Hyldahl, C.; Wulff, W. D. *J. Organomet. Chem.* **1987**, *334*, 9; Wulff, W. D.; Chan, K. S.; Tang, P. C. *J. Org. Chem.* **1984**, *49*, 2293.
4. (a) Zhou, G.; Corey, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 11958; (b) Noland, W. E.; Kedrowski, B. L. *Org. Lett.* **2000**, *2*, 2109; (c) Catellino, A.; Rapoport, H. *J. Org. Chem.* **1986**, *51*, 1006; (d) Shisido, K.; Bando, T. *J. Mol. Catal. B: Enzym.* **1998**, *5*, 183; (e) Bando, T.; Shisido, K. *Synlett* **1997**, 665; (f) Pirrung, M. C.; Lee, Y. R. *Tetrahedron Lett.* **1996**, *37*, 2391; (g) Koreeda, M.; Dixon, L. A.; Hsi, J. D. *Synlett* **1993**, 556; (h) Horne, S.; Weeratunga, G.; Rodrigo, R. *J. Chem. Soc., Chem. Commun.* **1990**, 39; (i) Horne, S.; Weeratunga, G.; Rodrigo, R. *J. Chem. Soc., Chem. Commun.* **1988**, 1006; (j) Roberts, J. C.; Sheppard, A. H.; Knight, J. A.; Roffey, P. *J. Chem. Soc. (C)* **1968**, 22.
5. Prepared using a modification of Raucher's procedure see: Raucher, S.; Bray, B. L. *J. Org. Chem.* **1987**, *52*, 2332, and also Ref. 7a.
6. Davies, M. W.; Johnson, C. N.; Harrity, J. P. A. *J. Org. Chem.* **2001**, *66*, 3525; For seminal studies see: Wulff, W. D.; Tang, P. C.; McCullum, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 7677; Dötz, K. H.; Muhlemeier, J.; Schubert, U.; Orama, O. *J. Organomet. Chem.* **1983**, *247*, 187; Yamashita, A.; Toy, A. *Tetrahedron Lett.* **1986**, *27*, 3471.
7. (a) Harrity, J. P. A.; Kerr, W. J.; Middlemiss, D.; Scott, J. S. *J. Organomet. Chem.* **1997**, *532*, 219; (b) Yamashita, A.; Toy, A.; Ghazal, N. B.; Muchmore, C. R. *J. Org. Chem.* **1989**, *54*, 4481; Bauta, W. E.; Wulff, W. D.; Pavkovic, S. F.; Zaluzec, E. J. *J. Org. Chem.* **1989**, *54*, 3249; Yamashita, A.; Toy, A.; Scahill, T. A. *J. Org. Chem.* **1989**, *54*, 3625; Yamashita, A.; Scahill, T. A.; Toy, A. *Tetrahedron Lett.* **1985**, *26*, 2969; Yamashita, A. *J. Am. Chem. Soc.* **1985**, *107*, 5823; Yamashita, A.; Scahill, T. A.; Chidester, C. G. *Tetrahedron Lett.* **1985**, *26*, 1159; Flitsch, W.; Lauterwein, J.; Micke, W. *Tetrahedron Lett.* **1989**, *30*, 1633; For ynol ether surrogates see: Anderson, J. C.; Denton, R. M.; Hickin, H. G.; Wilson, C. *Tetrahedron* **2004**, *60*, 2327.
8. See: Civitello, E. R.; Rapoport, H. *J. Org. Chem.* **1994**, *59*, 3775.
9. For previous syntheses of this compound see: (a) Malanga, C.; Mannuci, S.; Lardicci, L. *J. Chem. Res. (S)* **2001**, 97; (b) Brunetière, A. P.; Lallemand, J. Y. *Tetrahedron Lett.* **1988**, *29*, 2179; (c) Pezechk, M.; Brunetière, A. P.; Lallemand, J. Y. *Tetrahedron Lett.* **1986**, *27*, 3715.
10. Quayle, P. In *Comprehensive Organic Functional Group Transformations*; Moody, C. J., Ed.; Pergamon: Oxford, 1995; Vol. 5, Chapter 25, pp 931–960; Timko, J. M.; Yamashita, A. *Org. Synth.* **1993**, *71*, 72; Semmelhack, M. F. In *Organometallics in Organic Synthesis: A Manual*, 2nd ed.; Schlosser, M., Ed.; Wiley: Chichester, 2002; Chapter 9, pp 1024–1042.
11. Boeckman, R. K.; Bruza, K. J. *Tetrahedron Lett.* **1977**, *18*, 4187; Boeckman, R. K.; Bruza, K. J. *Tetrahedron* **1981**, *37*, 3997; Metallation of cyclic vinyl ethers can be capricious, see: Milne, J. E.; Kocienski, P. J. *Synthesis* **2003**, 584; for reviews see: Chinchilla, R.; Najera, C.; Yus, M. *Chem. Rev.* **2004**, *104*, 2667; Friesen, R. W. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1969; Metallation of dihydrofurans with this oxygenation pattern has little precedent; see: Boeckman, R. K.; Jayaram, R.; Johnston, B. H. *Heterocycles* **1987**, *25*, 33; Schreiber, S. L.; Porco, J. A. *J. Org. Chem.* **1989**, *54*, 4721.
12. Dulcère, J.-P.; Crandall, J.; Faure, R.; Santelli, M.; Agati, V.; Mihoubi, M. N. *J. Org. Chem.* **1993**, *58*, 5702, and references cited therein.
13. Ghosh, A. K.; Kincaid, J. F.; Walters, D. E.; Chen, Y.; Chaudhuri, N. C.; Thompson, W. J.; Culberson, C.; Fitzgerald, P. M. D.; Lee, H. Y.; McKee, S. P.; Munson, P. M.; Duong, T. T.; Darke, P. L.; Zugay, J. A.; Schleif, W. A.; Axel, M. G.; Lin, J.; Huff, J. R. *J. Med. Chem.* **1996**, *39*, 3278.
14. For sporadic reports see: Yanada, R.; Koh, Y.; Nishimori, N.; Matsumura, A.; Obika, S.; Mitsuya, H.; Fujii, N.; Takemoto, Y. *J. Org. Chem.* **2004**, *69*, 2417; Chakraborty, A.; Marek, I. *Chem. Commun.* **1999**, 2375; Woltering, T. J.; Hoffmann, H. M. R. *Tetrahedron* **1995**, *51*, 7389; Lynch, M. J.; Simpson, J.; Weavers, R. T. *Aust. J. Chem.* **1993**, *46*, 203; Ichinose, Y.; Matsunaga, S.; Fugami, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1989**, *30*, 3155.
15. Okabe, M.; Abe, M.; Tada, M. *J. Org. Chem.* **1982**, *47*, 1775.
16. Bamford, W. R.; Stevens, R. R. *J. Chem. Soc.* **1952**, 4735.
17. The Bamford–Stevens reaction has found scant application in the synthesis of dihydrofurans: (a) Gianturco, M. A.; Friedel, P.; Flanagan, V. *Tetrahedron Lett.* **1965**, *6*, 1847; (b) Brunetière, A. P.; Leclaire, M.; Bhatnagar, S.; Lallemand, J. Y.; Cossy, J. *Tetrahedron Lett.* **1989**, *30*, 341; (c) Smith, A. B.; Sulikowski, G. A.; Fujimoto, K. *J. Am. Chem. Soc.* **1989**, *111*, 8039.
18. In order to account for the regioselectivity observed in the formation of **15** we speculate that this product derives from a competing pathway involving nucleophilic attack at the carbene by the electron rich acetylene **5**. Electrocyclization of **i** leads to **ii**, which on purification results in the isolation of the by-product **15**. The inorganic chromium complex ($S{\cdot}Cr(CO)_5$) generated in this sequence is presumably also able to participate in a [2+2+1] reaction with **5** affording the cyclopentadienone **iii**, which evidently suffers reduction under the reaction conditions to cyclopentenone **16**.
The moderate yield observed in the key benzannulation step (31%) presumably reflects the fine balance between the desired transformation and a miriad of other possible pathways in this case. For related group 6-mediated [2+2+1] cycloadditions of *eneynes* see: Hoye, T. R.; Suriano, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 1154. The [2+2+1] cycloaddition of ynol ethers with alkynes also has literature precedent (Imbriglio, J. E.; Rainier, J. D. *Tetrahedron Lett.* **2001**, *42*, 6987). Herndon (Herndon, J. W.; Patel, P. P. *Tetrahedron Lett.* **1997**, *38*, 59) has reported the reduction of cyclopentadienones by 'Cr(0)' in



the presence of a proton source. The formation of cyclopentenones during Dötz reactions also has literature precedent (Yamashita, A.; Toy, A.; Watt, W.; Muchmore, C. R. *Tetrahedron Lett.* **1988**, *29*, 3403).

19. Moser, W. H.; Sun, L.; Huffman, J. C. *Org. Lett.* **2001**, *3*, 3389; Fogel, L.; Hsung, R. P.; Wulff, W. D.; Sommer, R. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **2001**, *123*, 5580; Chamberlin, S.; Wulff, W. D. *J. Org. Chem.* **1994**, *59*, 3047.
20. Muslin, D. V.; Lyapina, N. S.; Tyulina, N. E.; Khorshev, S. Y.; Vavilina, N. N. *Zh. Obshch. Khim.* **2001**, *71*, 1322; Cooper, G. D. *J. Org. Chem.* **1961**, *26*, 925; Speier, J. L. *J. Am. Chem. Soc.* **1952**, *73*, 1003; For a review of Brook-type rearrangements see: Moser, W. H. *Tetrahedron* **2001**, *57*, 2065.
21. Saá, J. M.; Dopico, M.; Martorell, G.; García-Raso, A. *J. Org. Chem.* **1990**, *55*, 991.
22. Cacchi, S.; Ciattini, P. G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1986**, *27*, 5541.
23. Representative analytical data: Compound **2**: mp 148–150 °C, ν_{max} (film) 3353 (br), 2954 (s), 2917 (s), 2848 (s), 2848 (s), 1625 (s), 1443 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.31 (1H, d, $J = 5.7$ Hz, H-8a), 6.03 (1H, d, $J = 1.8$ Hz, Ar–H), 5.90 (1H, d, $J = 1.8$ Hz, Ar–H), 4.80 (1H, br s, OH), 4.11–4.04 (1H, m, H-2), 4.01–3.94 (1H, m, H-3a), 3.70 (3H, s, OMe), 3.68–3.60 (1H, m, H-2), 2.20–2.07 (2H, m, H-3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 160.2, 150.9, 110.4, 103.8, 93.3, 87.0, 65.9, 54.0, 42.5, 29.9; *m/z* (CI) 208 (M^+, 20%), 209 ($[M+H]^+$, 100%), found M^+ 208.0735; $C_{11}H_{12}O_4$ requires M^+ 208.0736.
Compound **3**: mp 110–111 °C; ν_{max} (film) 3416, 2948, 2886, 2855, 1596 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.38 (1H, d, $J = 5.9$ Hz, H-8a), 5.02 (1H, s, OH), 4.18–4.08 (3H, m, H-2, OCH_2CH_3), 4.05–3.96 (1H, m, H-3a), 3.87 (3H, s, OCH_3), 3.80–3.70 (1H, m, H-2), 2.23–2.15 (2H, m, H-3), 1.35 (3H, t, $J = 7.0$ Hz, OCH_2CH_3), 0.92 (9H, s, Si–$(CH_3)_3$), 0.42 (3H, s, Si–CH_3), 0.40 (3H, s, Si–CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 154.9, 152.4, 129.5, 112.8, 109.8, 106.2, 68.7, 67.8, 60.9, 45.0, 31.6, 27.1, 27.0, 18.6, 15.8, −1.5, −1.7 ppm; *m/z* (CI) 367 ($[M+H]^+$, 100%); found C 61.71%, H 8.15%; M^+ 366.1866, $C_{19}H_{30}O_5\ ^{29}Si$ requires C 62.26%, H 8.25%; M^+ 366.1862.
Compound **4**: mp 57–63 °C; ν_{max} (film) 2961 (m), 2876 (m), 2060 (m), 1993 (w), 1929 (s), 1725 (w), 1574 (w), 1214 (m), 1021 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.25 (1H, d, $J = 5.6$ Hz, H-6a), 5.40 (1H, d, $J = 3.6$ Hz, H-3), 5.20–5.08 (2H, q, $J = 7.0$ Hz, OCH_2CH_3), 4.11 (1H, app. t, $J = 8.1$ Hz, H-5), 3.85–3.75 (1H, m, H-5), 3.75–3.65 (1H, m, H-3a), 2.15–2.05 (1H, m, H-4), 1.96–1.88 (1H, dd, $J = 4.3$, 11.7 Hz, H-4), 1.68–1.60 (3H, t, $J = 7.0$ Hz, OCH_2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 324.2, 225.0, 216.7, 164.1, 109.7, 103.3, 76.6, 67.1, 47.7, 47.4, 31.5, 15.4 ppm; found C 46.58%, H 3.48%; $C_{14}H_{12}O_8Cr$ requires C 46.68%, H 3.36%.
24. For representative examples see: Che, Y.; Gloer, J. B.; Scott, J. A.; Malloch, D. *Tetrahedron Lett.* **2004**, *45*, 6891, and references cited therein.