Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters
Tetrahedron Letters 47 (2006) 6627–6633

Toward aflatoxin B2: an unexpected additive effect in a Dötz benzannulation reaction

Stephen A. Eastham,[a] John Herbert,[b] Steven P. Ingham,[a] Peter Quayle[a,*] and Matthew Wolfendale[a]

[a]*School of Chemistry, The University of Manchester, Manchester M13 9PL, UK*
[b]*Sanofi-Aventis, Alnwick Research Centre, Willowburn Drive, Alnwick NE66 2JF, UK*

Received 12 April 2006; revised 4 July 2006; accepted 6 July 2006
Available online 1 August 2006

Abstract—The addition of tolane to an intermolecular Dötz reaction has a profound effect upon the product distribution of the reaction such that cyclopentannulation becomes a major pathway rather than benzannulation. In addition the incorporation of an electron-rich acetylene into the cyclopentannulated product proceeds in a contra-steric fashion, a set of results which has been rationalised in terms of the reversible formation of intermediate π-complexes at the branch point of the benzannulation sequence.

In a recent letter,[1] we reported an approach to the synthesis of aflatoxin B2 based upon a Dötz benzannulation reaction.[2] In this initial study, we observed that mild thermolysis of carbene complex **1** in the presence of the oxygenated acetylene **2** (2.0 equiv) took place in refluxing THF affording the benzannulated product **3** in 31% yield after chromatography. Minor by-products of this reaction included the cyclopentenones **4** (ca. 1%) and **5** (<1%), although the alternate benzannulation product **6** was not observed. The silane **3** was subsequently converted to **7**, a key intermediate in the synthesis of aflatoxin B2, via a regioselective 1,3-silatropic rearrangement, Scheme 1.

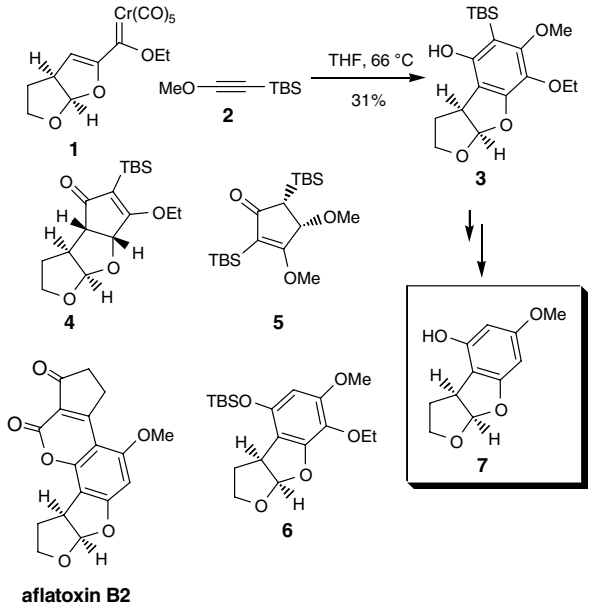
Whilst cyclopentenone byproducts have been observed[3] previously during the Dötz benzannulation reactions of alkoxycarbene complexes, their occurrence during the benzannulation reactions of simple *vinyl* carbene complexes are uncommon[4] and less frequently a complication than in the case of the Dötz reactions of aryl carbene complexes. The isolation of **5**, via a formal reductive carbonylation of acetylene **2** is, to our knowledge, without precedent during the course a Dötz reaction.[5] In addition the regiochemical outcome of the cyclopentannulation reaction is opposite to that expected from earlier studies which have been rationalised in terms of steric effects.[2c]

As a continuation of this work we wished to develop a convergent route to the synthesis of aflatoxin B2 based upon a tandem Dötz benzannulation–cyclisation sequence which required optimisation of the key Dötz reaction.

In an effort to map out the generality, if any, of the Dötz reactions of **1** we briefly investigated its reactions with simple acetylenes. Hence, exposure of **1** to phenyl acetylene (2.5 equiv; THF, 66 °C; 16 h) afforded the phenol **8** in moderate overall yield (38%) after column chromatography.[6] More interestingly reaction of **1** with the malonate derivative **9** (2.5 equiv; THF, 66 °C; 16 h) followed by the addition of DBU (5 equiv; THF; 30 min; 20 °C) led directly to the δ-lactone **10**, as a 1:1 mixture of diastereoisomers, in 32% overall yield, and serves as a useful model reaction for the installation of the **A**–**D** rings of aflatoxin B2. The benzannulation chemistry of the methoxy carbene complex **11** mirrors, to a large extent, the reactivity of **1**. Hence mild thermolysis of **11** in THF in the presence of either **2** or phenyl acetylene affords the benzannulated products **12** and **13** in 26% and 29% yields, respectively.[7] On this occasion the ester **14**, the formal oxidation product of **11** was also isolated (16% yield) which we presume arose from oxidation of unreacted carbene complex during work-up. Most significantly, substitution of phenyl acetylene by tolane in this particular reaction resulted in a dramatic increase

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

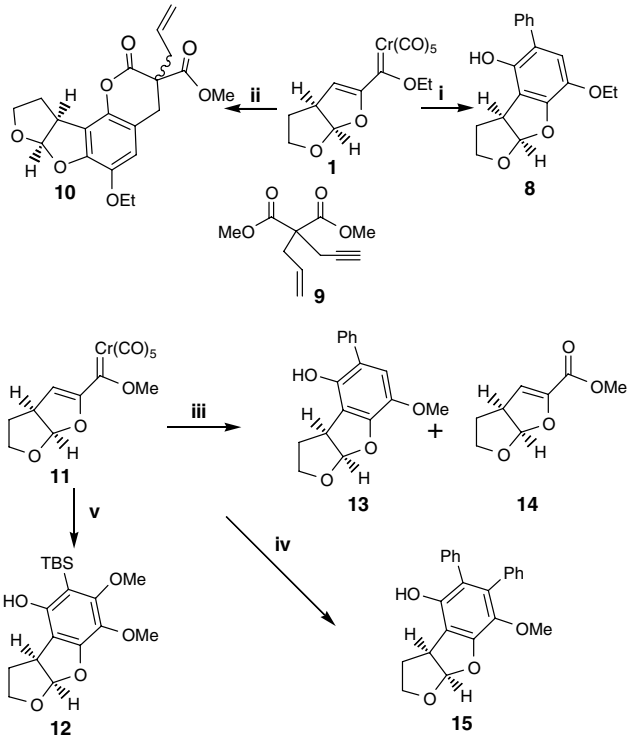
0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.07.041



Scheme 1. Dötz benzannulation approach to aflatoxin B2.1.

in reaction efficiency and afforded the phenol **15** in 90% yield after chromatography, Scheme 2. This result suggests that tolane is a particularly good substrate in these benzannulation reactions and is an observation which was to gain greater significance in subsequent studies.

As we were initially interested in the reaction between carbene complex **1** and the alkyne **2**, optimisation of this reaction became our prime concern. Curiously, and in contrast to the usual positive dependence of benzannulated product upon alkyne concentration[8] (the so-called '*Allochemical Effect*'), we noted that in this particular case, increasing the concentration of the alkyne **2** with respect to **1** (ratio of **1**:**2** increased from 1:2.5 to 1:4; $[\mathbf{1}] = 0.06$ mol dm^{-3}), in THF as solvent, led to a diminution in yield of the phenol **3** together with a concomitant increase in the formation of cyclopentenone **4**. Changing the solvent from THF (**3**:**4** = 15:1) to the less basic ethyl acetate (ratio of **1**:**2** = 1:4) resulted in a higher overall conversion (48%), an outcome which can largely be attributed to the increased amount of cyclopentenone **4** now formed during the reaction (**3**:**4** = 2:1).[9] The use of higher boiling, non-polar solvents (e.g., toluene) not unsurprisingly led to the direct formation[10] of the silyl ether **6** (28%) together with an enhanced yield of the cyclopentenone **4** (18%). The yield of the cyclopentenone **5** was uniformly low (up to a 4% maximum) in all of these reactions, Table 1.



Scheme 2. Reagents and conditions: (i) PhCCH (2.5 equiv); THF; 66 °C; (ii) a. **9** (2.5 equiv); THF; 66 °C; b. DBU (5 equiv); THF; 20 °C; (iii) PhCCH (2 equiv); THF; 66 °C; (iv) Tolane (2 equiv); THF; 66 °C; (v) **2** (2.5 equiv); THF; 66 °C.

The use of dry state adsorption techniques[11] (DSA) can, in certain cases, have a beneficial effect on the efficiency of Dötz reactions and we wondered what effect these conditions would have in this particular context. Unfortunately adopting Kerr's technique to the reaction between **1** and **2** resulted in a lowering of the overall yield of the reaction although, once again, the relative proportion of cyclopentannulated products compared to benzannulated products again increased (**6**:[**4**+**5**] = 3:5). As in the case of toluene as solvent, in situ rearrangement of the initial benzannulation product **3** to the silyl ether **6** was again observed under DSA conditions.

Whilst we were encouraged by the result of the tandem Dötz-cyclisation reaction leading from **1** to **10** it appeared that the benzannulation reactions of **1** and **11** with electron-rich or terminal acetylenes proceeded in only moderate yields. The results from the DSA reac-

Table 1. Benzannulation reactions of carbene complexes **1** and **11**[a]

Solvent	Carbene;alkyne ([alkyne]:[carbene])	Temperature (°C)	Product (%)
THF	**1**; **2** (2.5)	66	**3** (31)
			4 (ca. 1)
THF	**1**; **2** (4)	66	**3** (14)
			4 (3)
EtOAc	**1**; **2** (4)	80	**3** (32)
			4 (16)
Toluene	**1**;**2** (4)	110	**6** (28)
			4 (18)
DSA (silica gel)	**1**; **2** (4)	100	**6** (12)
			4 (15)
			5 (4)
THF	**1**; Phenylacetylene (2.5)	66	**8** (38)[b]
THF	**1**; **9** (2.5)	66	**10** (32)[b]
THF	**11**; **2** (2.5)	66	**12** (26)[b]
THF	**11**; Phenylacetylene (2)	66	**13** (29)
			14 (16)
THF	**11**; Tolane (2)	66	**15** (90)
THF	**1**; Tolane (5); **2** (2)	66	**15** (44)
			3 (<1)
			4 (15)

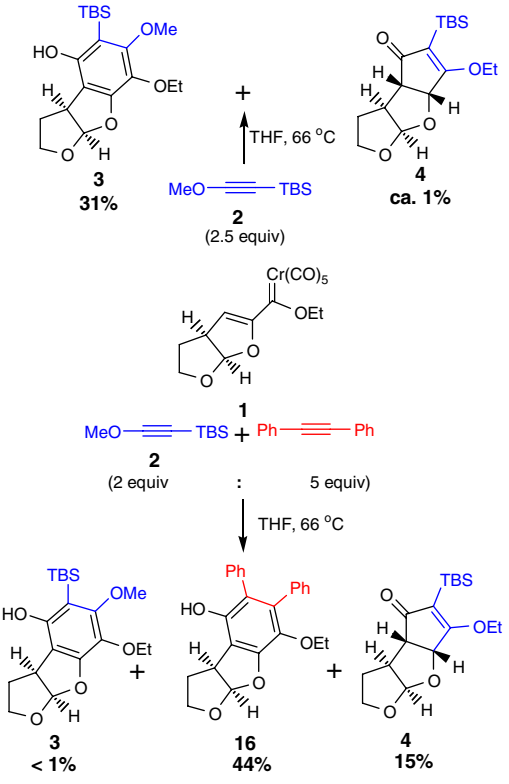
[a] All reactions were conducted under anaerobic conditions. Reagents and solvents were degassed prior to thermolysis. The concentration of **1** was kept to 0.06–0.07 mol dm^{-3} (where appropriate).
[b] The remainder of the mass balance proved to be intractable.

tions in particular suggested to us that the stabilisation of coordinately unsaturated species, formed during the initial phases of the reaction sequence, may well be important if higher yields of benzannulated products were to be obtained. We decided to test this hypothesis by adding tolane to a reaction mixture comprising of **1** and **2** (**1**:**2** = 1:2) prior to thermolysis in THF. This notion is based on the precedent cited by Finn[12] who reported that the efficiency of *intramolecular* Dötz benzannulation reactions can be increased merely by the addition of tolane. In the case of Finn's study, incorporation of tolane into the product was not observed as its presumed role was that of a labile ligand which could temporarily stabilise potentially reactive, coordinately unsaturated, intermediates (the '*Xenochemical Effect*').

To our knowledge the efficacy of the xenochemical effect in *intermolecular* Dötz reactions has not been evaluated, hence the motivation behind this investigation. The results from our initial study were surprising: mild thermolysis of carbene **1** (0.07 mol dm^{-3} in THF; 66 °C) in the presence of tolane (5 equiv) and the alkyne **2** (2 equiv) afforded the benzannulated product **16** (44%) and the cyclopentenone **4** (15%) after column chromatography, Scheme 3. Significantly we were unable to detect the presence of the desired benzannulation product **3** in the ^{1}H NMR spectrum of the crude reaction mixture. This result is intriguing given that:

(i) the benzannulation reaction between alkyne **2** and **1** (vide supra) affords **3** as the major product (**2**:**1** >30:1) under comparable conditions, and
(ii) the benzannulated product **15** is isolated in very high yields from the reaction of **11** with tolane alone.

Any explanation of these results also has to take into account the abnormal regiochemical course observed in the incorporation of alkyne **2** into cyclopentenone **4**.



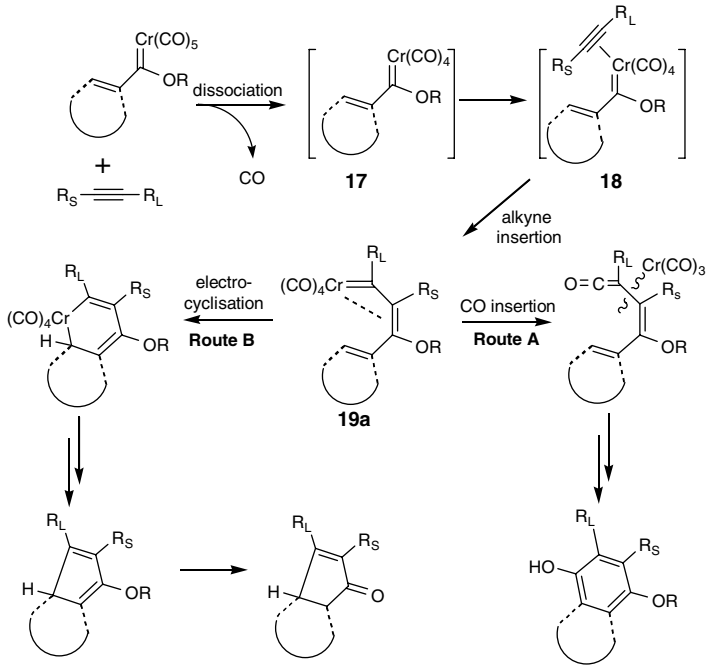
Scheme 3. Divergent benzannulation/cyclopentannulation pathways: effect of added alkyne.

Whilst there is still much discussion[13] concerning the precise mechanistic detail of the Dötz reaction it is generally accepted that the isolation of the products of benzannulation (route **A**) and cyclopentannulation (route **B**) stems from a common intermediate **19a** where the rate determining step in the overall sequence is loss

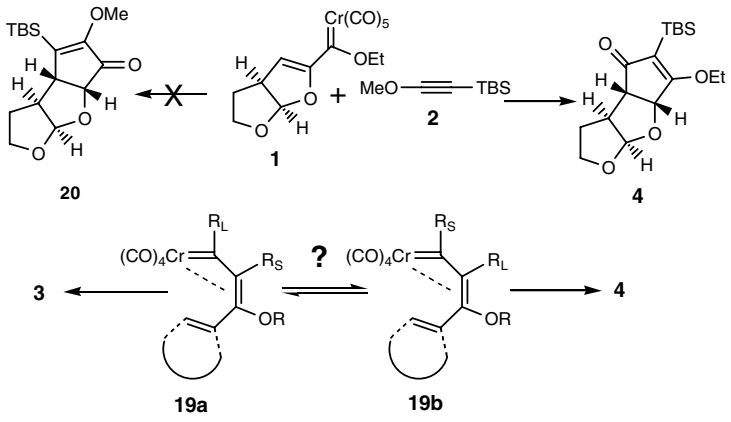
of a CO ligand from the initial chromium pentacarbonyl complex **1** to the **16e** species **17**.[14]

It has been argued[15] that regiochemical issue arising from the benzannulation and cyclopentannulation pathways is controlled during the initial formation of the η^1,η^3-vinyl complex **19a** where the more sterically demanding residue (R_L) is incorporated proximal to the metal fragment, Scheme 4. In our reactions in which no additional alkyne, other than **2**, was added to the reaction mixture it should be noted therefore that whilst the regiochemistry of incorporation of the alkyne **2** into the benzannulated product **3** is in accord with this steric argument, its incorporation into the cyclopentannulated product **4** proceeds in the regio-reversed sense. If **19a** were to be a common intermediate for the formation of both the benzannulated and cyclopentannulated products it follows that formation of the regioisomeric cyclopentenone **20** rather than **4** would be expected. As far as we can tell, cyclopentenone **4**[16] appears to be the major product of the cyclopentannulation pathway which is therefore at odds with the currently accepted rationalisation for the regiochemistry cyclopentenone formation.[17a] If **19a** were to serve as the branch point in the formation of both **3** and **4** then **19a** would be required to be in equilibrium with the isomeric complex **19b**, Scheme 5. Furthermore in order to explain the product distribution in the absence of added tolane, benzannulation of **19a** and cyclopentannulation of **19b** would be required to be more favourable than benzannulation of **19b** and cyclopentannulation of **19a**.

This situation is further complicated by the addition of tolane whose presence wholly suppresses the benzannulation route of alkyne **2** leading to **3** whilst the cyclopentannulation route to **4** is still accessible, that is, in this case all benzannulation/cyclopentannulation reactions other than those leading to **4** and **16** are apparently



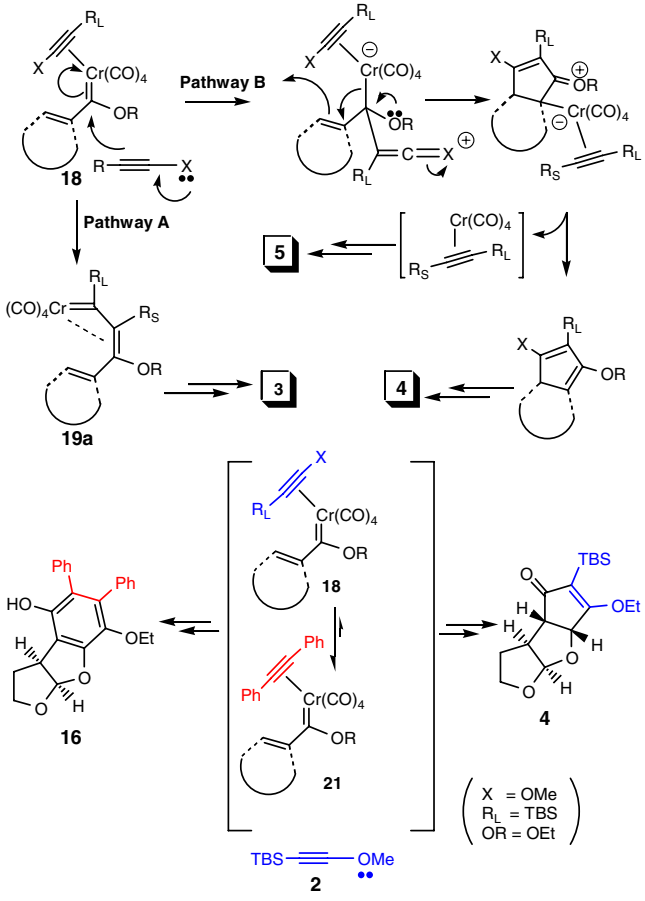
Scheme 4. Generalised benzannulation/cyclopetannulation sequence.[14,15]



Scheme 5. Basic mechanistic conundrum.

disfavoured. Whilst there is some evidence[17c] to suggest that the interconversion of η^1,η^3-vinyl complexes such as **19a,b** is possible we would like to put forward an alternate explanation for our results which also has relevance to a number of related observations in the literature.

We posit that the initial reaction pathway is as originally proposed by Dötz. In the case where *only* alkyne **2** is present (rate limiting?) loss of carbon monoxide from **1**, generating the **16e** complex **17** followed by co-ordination with added alkyne **2** affords the π-complex **18**.[18] At this stage we suggest that two different pathways could be followed. Rearrangement of **18** to the η^1,η^3-vinyl complex **19a** (pathway A) would ultimately afford the benzannulated product **3**. However interception of the π-complex **18** via nucleophilic attack by an electron-rich alkyne at the carbene carbon could divert the reaction pathway to the cyclopentannulation route (i.e., leading ultimately to **4**) as depicted below, Scheme 6. The regiochemical outcome observed for pathway **B**, Scheme 6, is governed by the polarisation of the carbene/alkyne partners. In those cases where no other alkyne besides **1** is added, generation of the π-complex **18** would then lead to the formation of the benzannulated product **3** or the cyclopentenone **4**, respectively. In the case where a *mixture* of alkynes is present in the reaction mixture (e.g., tolane and **2**) the fact that little, or none, of the alternate benzannulation products **3** or **6** are produced may suggest that the equilibrium between the two π-complexes **18** and **21**, is in favour of **21**. Partitioning of **21** would therefore lead to the benzannulated product **16** (Dötz process) or the cyclopentenone **4**. The ratio of products **16**:**4** observed from this reaction will therefore be dependent both upon the rates of formation of the two possible π-complexes **18** and **21** and their subsequent intramolecular rearrangement (Dötz) or intermolecular capture (cyclopentannulation) by **2**.



Scheme 6. Modified Dötz/cyclopentannulation mechanism.

In support of this hypothesis we note that alkynyl thioethers also undergo cyclopentenone formation[19] with the same regiochemistry as found in this study where again it appears that simple steric arguments again do not pertain. Similar electronic effects may also be used to explain the 'contrasteric' outcome observed in the reactions of alkynylstannanes/boranes[20] in the Dötz benzannulation reaction. Here we muse whether the well known[21] electronic effect on the tin residue (i.e., stabilisation of a β-carbocation) has a controlling influence on the regiochemical outcome of these particular reactions. In addition it is known that Fischer carbene complexes react with carbon nucleophiles such as enolate anions,[22] enamines[23] and acetylide anions[24] at the electron deficient carbene carbon and it is not unreasonable therefore that, in certain cases, attempted benzannulation/cyclopentannulation reactions may be forced down this pathway using electron-rich alkynes.

In conclusion, we suggest that the branch point for the benzannulation/cyclopentannulation of electron-rich alkynes in the Dötz reaction may, in certain cases, be at the π-complex stage **18** prior to rearrangement to the η^1,η^3-vinyl complex **19a** (Scheme 6). The result of an intermolecular competition experiment raises the possibility that the addition of alkynes[25] to the reaction mixture may divert the pathway of the Dötz/cyclopentannulation process, the controlling element being the relative affinity of the individual alkynes for the unsaturated metal centre. Synthetic applications and mechanistic aspects of this effect are currently in progress.

Acknowledgements

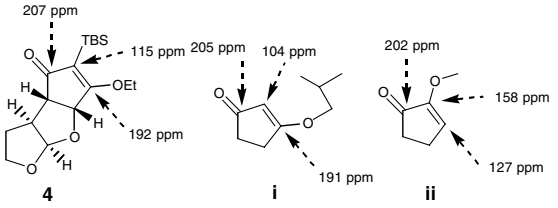
We thank Sanofi-Aventis and the EPSRC for support of this work.

References and notes

1. Eastham, S. A.; Ingham, S. P.; Hallett, M. R.; Herbert, J.; Quayle, P.; Raftery, J. *Tetrahedron Lett.* **2006**, *47*, 2299–2304.
2. (a) Dötz, K. H.; Wenzel, B.; Jahr, H. C. *Topics Curr. Chem.* **2005**, *248*, 63–103; Minatti, A.; Dötz, K. H. *Topics Organomet. Chem.* **2004**, *13*, 123–156; For an overview of recent developments in this area, see: Barluenga, J.; Fernández-Rodríguez, M. A.; Aguilar, E. *J. Organomet. Chem.* **2005**, *690*, 539–587; For mechanistic studies, see: (b) Barluenga, J.; Aznar, F.; Gutiérrez, I.; Martín, A.; Garcia-Granda, S.; Llorca-Baragaño, M. A. *J. Am. Chem. Soc.* **2000**, *122*, 1314–1324; Torrent, M.; Duran, M.; Solà, M. *Chem. Commun.* **1998**, 999–1000; Solá, M.; Duran, M.;

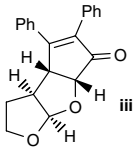
Torrent, M. *Catal. Metal Complexes* **2002**, *25*, 269–287; Fischer, H.; Hofmann, P. *Organometallics* **1999**, *18*, 2590–2592; Torrent, M.; Duran, M.; Solà, M. *J. Am. Chem. Soc.* **1999**, *121*, 1309–1316; Hofmann, P.; Hämmerle, M.; Unfried, G. *New J. Chem.* **1991**, *15*, 769–789; Hofmann, P.; Hämmerle, M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 908–910; Gleichmann, M. M.; Dötz, K. H.; Hess, B. A. *J. Am. Chem. Soc.* **1996**, *118*, 10551–10560; Cases, M.; Frenking, G.; Duran, M.; Solà, M. *Organometallics* **2002**, *21*, 4182–4191; For the regiochemical outcome from alkoxyacetylenes in Dötz reactions, see (c) King, J.; Quayle, P.; Malone, J. F. *Tetrahedron Lett.* **1990**, *31*, 5221–5224.

3. Yamashita, A.; Toy, A.; Watt, W.; Muchmore, C. R. *Tetrahedron Lett.* **1988**, *29*, 3403–3406; de Meijere, A.; Schirmer, H.; Duetsch, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 3964–4002; Wu, Y.-T.; Vidovic, D.; Magull, J.; de Meijere, A. *Eur. J. Org. Chem.* **2005**, 1625–1628; For overviews see: Dörwald, F. Z. *Angew. Chem., Int. Ed.* **2003**, *42*, 1332–1334; Herndon, J. W. *Tetrahedron* **2000**, *56*, 1257–1280.
4. For an extensive study, see Wulff, W. D.; Bax, B. M.; Brandwold, T. A.; Chan, K. S.; Gilbert, A. M.; Hsung, R. P.; Mitchell, J.; Clardy, J. *Organometallics* **1994**, *13*, 102–126, This study also details the reactions of dihydropyranylchromium carbene complexes which prefer to undergo benzannulation rather than cyclopentannulation reactions with simple alkynes.
5. The synthesis of cyclopentenones via alternate transition metal reactions are however legion, see: Gibson, S. E.; Lewis, S. E.; Mainolfi, N. *J. Organomet. Chem.* **2004**, *689*, 3873–3890, and references therein.
6. Regiochemistry by anology.
7. The remainder of the mass balance proved to be an intractable mixture, however only one regiosisomer of the benzannulated product was observed.
8. Bos, M. E.; Wulff, W. D.; Miller, R. A.; Chamberlin, S.; Brandvold, T. A. *J. Am. Chem. Soc.* **1991**, *113*, 9293–9319.
9. The use of less polar solvents in such reactions usually results in an increase in benzannulation at the expense of cyclopentannulation as detailed in Ref. 4.
10. For related silicon migrations in Dötz reactions see: Ref. 1 and Moser, W. H.; Sun, L.; Huffman, J. C. *Org. Lett.* **2001**, *3*, 3389–3391; Fogel, L.; Hsung, R. P.; Wulff, W. D.; Sommer, R. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **2001**, *12*, 5580–5581; Chamberlin, S.; Wulff, W. D. *J. Org. Chem.* **1994**, *59*, 3047–3054.
11. Harrity, J. P. A.; Kerr, W. J.; Middlemiss, D. *Tetrahedron* **1993**, *49*, 5565–5576.
12. Gross, M. F.; Finn, M. G. *J. Am. Chem. Soc.* **1994**, *116*, 10921–10933.
13. To our knowledge there is only one other mention of a completion reaction in an *intermolecular* Dötz reaction, see: (a) Wulff, W. D. In *Advances in Metal-Organic Chemistry*; Liebskind, L. S., Ed.; JAI Press: London, 1988; Vol. 1, pp 356–357; In this case the regiochemistry of alkyne incorporation was inferred by analogy and not proven. For *intramolecular* capture of unsymmetrical diynes, see (b) Wulff, W. D.; Kaesler, R. W.; Peterson, G. A.; Tang, P.-C. *J. Am. Chem. Soc.* **1985**, *107*, 1060–1062.
14. For a discussion of the kinetics, see: Fischer, H.; Mühlemer, J.; Märkl, R.; Dötz, K. H. *Chem. Ber.* **1982**, *115*, 1355–1362; For an early overview of the mechanism of this reaction, see: Fischer, H.; Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587–608; For a review of the physical organic chemistry of this system, see: Bernasconi, C. F. *Adv. Phys. Org. Chem.* **2002**, *37*, 137–237.
15. Dötz, K. H.; Tomuschat, P. *Chem. Soc. Rev.* **1999**, *28*, 187–198.
16. Spectroscopic data: ν_{max} (film) 2952 (s), 2931 (s), 2888 (s), 2856 (s), 1685 (s), 1571 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.74 (1H, d, $J = 4.7$ Hz, H-7a), 5.35 (1H, d, $J = 6.3$ Hz, H-6a), 4.64–4.52 (1H, dq, $J = 7.2$, 9.8 Hz, $-OCH_2CH_3$), 4.44–4.32 (1H, dq, $J = 7.2$, 9.8 Hz, $-OCH_2CH_3$), 4.08–3.94 (2H, m, H-2), 3.10–3.02 (1H, m, H-3a), 2.98–2.92 (1H, dd, $J = 6.3$, 2.9 Hz, H-3b), 2.28–2.14 (1H, m, H-3), 2.00–1.90 (1H, m, H-3), 1.44–1.38 (3H, t, $J = 7.2$ Hz, $-OCH_2CH_3$), 0.90 (9H, s, Si^t*Bu*Me$_2$), 0.22 (3H, s, Si^{t}Bu*Me*$_2$), 0.21 (3H, s, Si^{t}Bu*Me*$_2$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.9, 192.4, 114.6, 111.2, 79.7, 67.9, 66.9, 57.3, 46.1, 33.3, 26.8, 17.9, 15.4, −5.3, −5.5 ppm; *m*/*z* (CI) 325 (MH^+, 28%); found: C, 62.84%; H, 8.64%; MH^+ 325.1835; $C_{17}H_{28}O_4Si$ requires: C, 62.92%; H, 8.70%; MH^+ 325.1828.The regiochemistry of the alkyne incorporation into **4** is readily apparent from the ^{13}C NMR data:



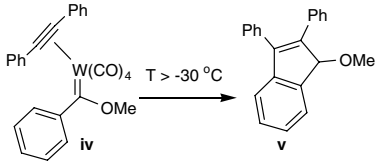
(cpd. i: Gulías, M.; Rodríguez, J. R.; Castedo, L.; Mascareñas, J. L. *Org. Lett.* **2003**, *5*, 1975–1977; cpd. ii: Buckley, D. J.; McKervey, M. A. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2193–2200).

17. (a) Wulff has noted, in one case,[17c,b] a similar regiochemical divergence between benzannulation and cyclopentannulation; (b) We were also unable to isolate any of the alternate cyclopentenone **iii** from this particular reaction.



(c) Waters, M. L.; Bos, M. E.; Wulff, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 6403–6413.

18. The formation of alkyne-chromium carbene chelate complexes has been documented Dötz, K. H.; Schäfer, T.; Kroll, F.; Harms, K. *Angew. Chem., Int. Ed., Engl.* **1992**, *31*, 1236–1238; Dötz, K. H.; Siemonet, S.; Hohmann, F.; Nieger, M. *J. Organomet. Chem.* **1997**, *541*, 285–290, as has the tungsten complex **iv**; Foley, H. C.; Strubinger, L. M.; Targos, T. S.; Geoffroy, G. L. *J. Am. Chem. Soc.* **1983**, *105*, 3064–3073, Interestingly π-complex **iv** is unstable and rearranges at temperatures above −30 °C to indene **v**:



19. Woodgate, P. D.; Sutherland, H. S.; Rickard, C. E. F. *J. Organomet. Chem.* **2001**, *627*, 206–220.
20. **Tin**: Chamberlin, S.; Waters, M. L.; Wulff, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 3113–3114; Eastham, S. A.; Herbert, J.; Painter, J. E.; Patel, P.; Quayle, P. *Synlett* **1998**, 61–63; Dötz, K. H.; Szesni, N.; Nieger, M.; Nattinen, K. *J. Organomet. Chem.* **2003**, *671*, 58–74;

Boron: Davies, M. W.; Johnson, C. N.; Harrity, J. P. A. *J. Org. Chem.* **2001**, *66*, 3525–3532; Anderson, J. C.; Denton, R. M.; Hickin, H. G.; Wilson, C. *Tetrahedron* **2004**, *60*, 2327–2335.

21. Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987.
22. For leading references see Barluenga, J.; Alonso, J.; Rodríguez, F.; Fañanás, F. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2460–2462; Barluenga, J.; Alonso, J.; Fañanás, F. J. *J. Am. Chem. Soc.* **2003**, *125*, 2610–2616.
23. Barluenga, J.; Ballesteros, A.; de la Rúa, R. R.; Santamaria, J.; Rubio, E.; Tomás, M. *J. Am. Chem. Soc.* **2003**, *125*, 1834–1842.
24. For overviews, see: Barluenga, J.; Flórez, J.; Fañanás, F. J. *J. Organomet. Chem.* **2001**, *624*, 5–17; Barluenga, J.; Martínez, S. *Arkivoc* **2006**, 129–147.
25. For the effects of additives in such reactions, see Flynn, B. L.; Schirmer, H.; Duetsch, M.; de Meijere, A. *J. Org. Chem.* **2001**, *66*, 1747–1754, and references cited therein.