Synthesis of polycyclic molecules *via* cascade radical carbocyclizations of dienynes: the first $SnPh_3$ radical-mediated [2 + 2 + 2] formal cycloaddition of dodeca-1,6-dien-11-ynes

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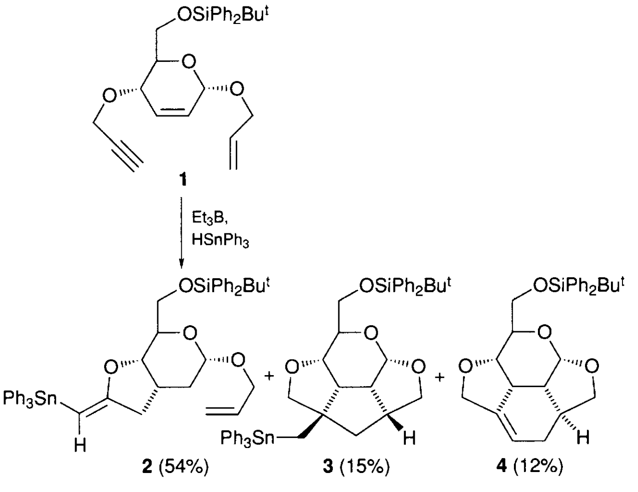
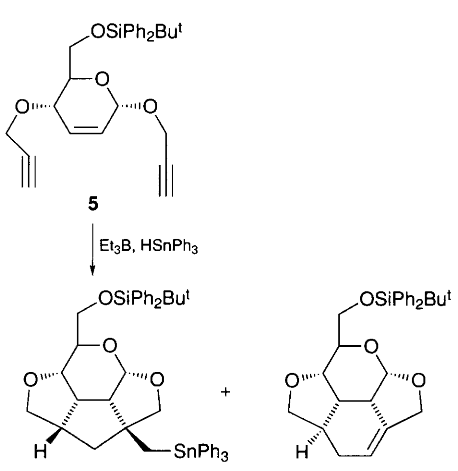
The dodeca-1,6-dien-11-ynes 1 and 5 give the polycyclic molecules 4 and 7, respectively, in the first known [2 + 2 + 2] cycloaddition reaction promoted by triphenyltin hydride, in a cascade free radical process.

In recent years cascade cyclizations have yielded elegant approaches to the synthesis of carbocycles.[1] In particular, metal-catalysed[2,3] cycloisomerization of enynes has become one of the best methods for the preparation of polycyclic molecules. In this context, radical ring closure[4] of terminal dienes has received much attention.[5] However, the free radical-promoted cycloisomerization of dienynes remains largely unexplored.[6] As a part of ongoing research into the synthesis of carbocycles using free radical-based methodologies,[7] I now report the first examples of a triphenyltin cascade radical-mediated cyclization of 4,9-dioxadodeca-1,6-dien-11-ynes.[8] As a result, I describe here the first formal free radical-promoted [2 + 2 + 2] cycloaddition of dienynes.



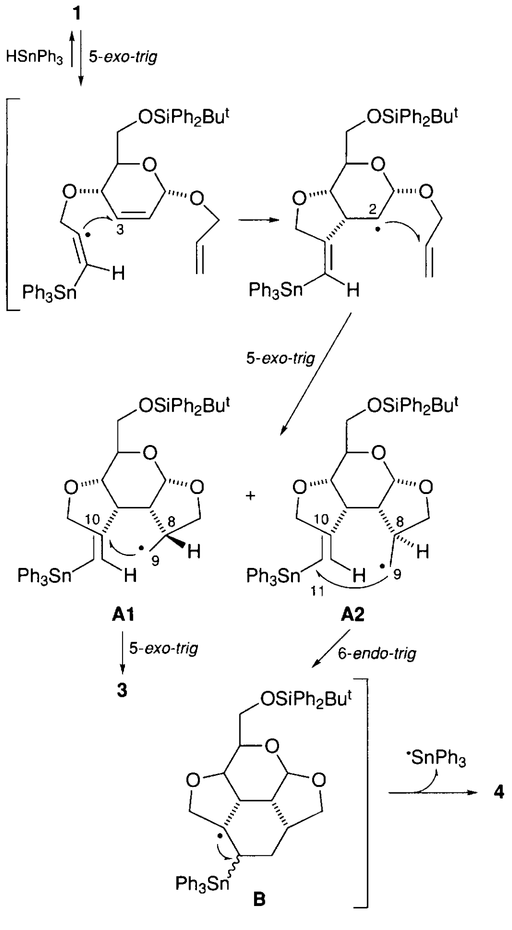
Scheme 1



Scheme 2

I began with dienyne sugar derivative **1**.‡ After treatment with triphenyltin hydride and triethylborane,§ pyranoside **2**[9] was obtained in 54% yield; in addition, we could detect and isolate products **3** and **4** (Scheme 1). These compounds, although obtained in low yield, represent new types of complex and enantiomerically pure 1,6-dioxatriquinanes and 1,6-dioxa-hydrindacenes,[5] respectively, that can be obtained from readily available chiral precursors. Each adduct was diastereomerically pure and the absolute configuration at the newly formed stereocentres was assigned by detailed 2D NOESY and ^1H NMR experiments.

The particular experimental conditions are critical; precursor **1** was recovered unaltered when warmed in toluene or treated with BEt_3 at room temperature, and reaction with palladium complexes[10] produced extensive decomposition.



Scheme 3

Encouraged by these results, I prepared the analogous prop-2-ynyl pyranoside **5**.‡ Using the same experimental conditions,§ a more complex reaction resulted; I could only purify and characterize the tris-annulated pyranosides **6** and **7**¶ (Scheme 2).

The unexpected formation of products **3**, **4**, **6** and **7** is a consequence of a series of three tandem radical cyclizations (Scheme 3). Compound **3** was obtained after hydrostannylation of the acetylene moiety, vinyl radical formation followed by 5-*exo-trig* cyclization at C-3 (sugar numbering), radical formation at C-2 and 5-*exo-trig* cyclization onto the terminal double bond; the resulting primary alkyl radical **A1** attacks the vinyltin moiety in a 5-*exo-trig* mode and the obtained radical traps hydrogen from $HSnPh_3$ leading to **3**, reinitiating the free radical chain reaction. In the case of compound **4** the same series of events gives the radical species **A2** which, after 6-*endo-trig* cyclization onto the pre-formed vinyltin function, gives species **B**; subsequent elimination generates the double bond at C-10–C-11; interestingly, the resulting triphenyltin radical re-initiates the chain reaction, *via* an overall addition–elimination type reaction,[11] in a catalytic manner.

From the yields and ratios of products **3** and **4**, and **6** and **7**, it is clear that while the 5-*exo-trig* radical cyclization from C-2 onto C-8 is not very selective, once the C-9 primary radical with H8 *exo* has been formed, it exclusively cyclizes in a 5-*exo-trig* mode that gives product **3**; note that this 5-*exo* path is particularly unfavourable because of the trisubstituted alkene in the vinyl moiety.[12] Similarly, when the C-9 primary radical with H8 *endo* has been formed, it exclusively cyclizes in a 6-*endo-trig* mode that gives product **4**. The same arguments can also be applied to the cyclization of precusor **5**. This extremely high selectivity is probably due to the particular steric and stereoelectronic constraints present in our rigid molecules.

Note that the formation of cyclohexenes **4** or **7** is the formal result of a triphenyltin hydride-mediated free radical-promoted [2 + 2 + 2] cycloaddition[13] of 4,9-dioxadodeca-1,6-dien-11-ynes. To our knowledge such a process has not been described before.

Footnotes

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‡ The synthesis of the radical precursors will be reported elsewhere.

§ In a typical procedure, the dienyne (0.77 mmol) is treated with triphenyltin hydride (1.1 mmol) and triethylborane (0.38 mmol) in toluene (0.016 M) at room temp. (these are typical conditions for hydrostannylation of acetylenes; see: K. Nozaki, K. Oshima and K. Utimoto, *J. Am. Chem. Soc.*, 1987, **109**, 2547). After 3–6 h, the solvent was removed and the residue submitted to flash chromatography. All new compounds showed good spectroscopic and analytical data.

¶ In the less polar fractions we could detect by ^1H NMR an analogous hydrostannylated product of type **2** (Scheme 1). We were unable to obtain it pure.

References

1 R. A. Bunce, *Tetrahedron*, 1995, **51**, 13 103.
2 B. M. Trost, *Acc. Chem. Res.*, 1990, **23**, 34.
3 K. P. C. Vollhardt, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 539.
4 B. Giese, *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon Press, New York, 1986; D. P. Curran, *Synthesis*, 1988, 417; C. P. Jasperse, D. P. Curran and T. L. Fevig, *Chem. Rev.*, 1991, **91**, 1237; W. B. Motherwell and D. Crich, *Free Radical Chain Reactions in Organic Synthesis*, Academic Press, London, 1991.
5 S. Hanessian and R. Léger, *J. Am. Chem. Soc.*, 1992, **114**, 3115 and references 1–5 cited therein.
6 M. Malacria, *Chem. Rev.*, 1996, **96**, 289; J. W. Grissom and B. J. Slattery, *Tetrahedron Lett.*, 1994, **35**, 5137.
7 J. Marco-Contelles, C. Destabel, P. Gallego, J. L. Chiara and M. Bernabé, *J. Org. Chem.*, 1996, **61**, 1354 and references cited therein.
8 The ability to add tin radicals to alkynes is well known: H. Pak, I. I. Canalda and B. Fraser-Reid, *J. Org. Chem.*, 1990, **55**, 3009; G. Stork and R. Mook, *J. Am. Chem. Soc.*, 1987, **109**, 2829.
9 N. Moufid, Y. Chapleur and P. Mayon, *J. Chem. Soc., Perkin Trans. 1*, 1992, 999.
10 B. M. Trost, G. J. Tanoury, M. Lautens, C. Chan and D. T. MacPherson, *J. Am. Chem. Soc.*, 1994, **116**, 4255; J.-F. Nguefack, V. Bolitt and D. Sinou, *Tetrahedron Lett.*, 1996, **37**, 59.
11 Y. Ueno, K. Chino and M. Okawara, *Tetrahedron Lett.*, 1982, **23**, 2575; W. B. Motherwell, A. M. K. Pennell and F. Ujjainwalla, *J. Chem. Soc., Chem. Commun.*, 1992, 1067.
12 A. L. J. Beckwith and C. H. Schiesser, *Tetrahedron*, 1985, **41**, 3925.
13 N. E. Schore, in *Comprehensive Organic Synthesis*, ed B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 5, ch. 9.4.

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