Radical Cyclisation of Bromomethyldimethylsilyl Propynyl Ethers; Serial Radical Cyclisations leading to a Hydrindene Framework from an Acyclic Substrate, Stereoselectively

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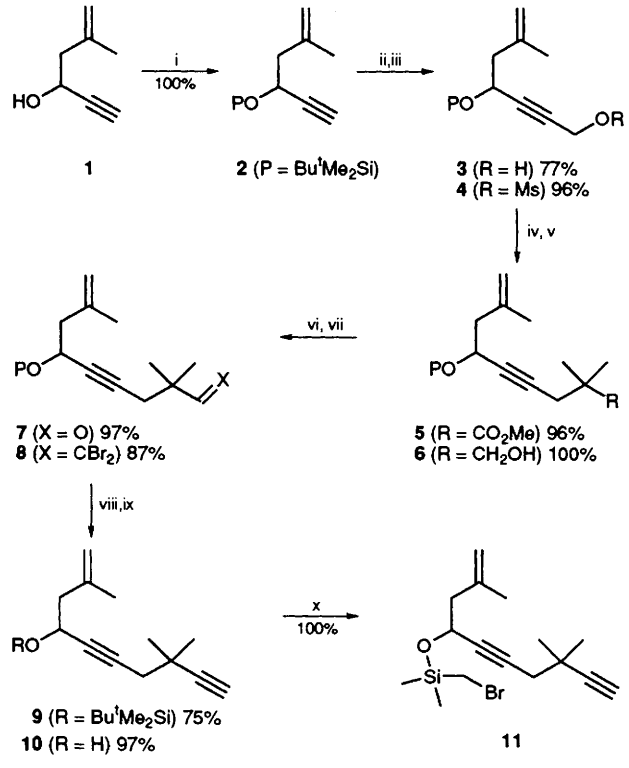
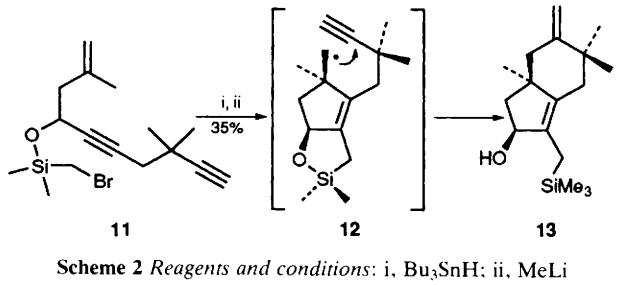
4-Bromomethyldimethylsiloxy-2,8,8-trimethyldec-1-en-5,9-diyne **11** is prepared and its radical cyclisation leads to a stereoselective synthesis of a hydrindene framework **13** *via* three consecutive 5-*exo-dig*, 5-*exo-trig* and 6-*exo-dig* radical processes.

The development of new synthetic routes to efficient syntheses of elaborate polycyclic frameworks from acyclic polyunsaturated compounds has attracted considerable interest.[1] The radical cyclisation of bromomethyldimethylsilyl propynyl ethers is a powerful reaction with a very effective control of regio-, chemo- and stereo-selectivity which allowed us to synthesize a diquinane in a one-pot reaction from an acyclic substrate.[2]



Scheme 1 *Reagents and conditions*: i, TBDMSCl, Et_3N, 4-DMAP; ii, Bu^{n}Li, $(CH_2O)_n$; iii, MsCl, Et_3N; iv, LDA, $(Me)_2CHCO_2Me$; v, $LiAlH_4$; vi, $(COCl)_2$, DMSO, Et_3N; vii, CBr_4, PPh_3; viii, Bu^{n}Li; ix, Bu$^n_4$NF; x, $(Me)_2CH_2BrSiCl$, Et_3N, 4-DMAP



Scheme 2 *Reagents and conditions*: i, Bu_3SnH; ii, MeLi

We report here the preparation of the acyclic precursor **11** and its radical cyclisation. The synthesis of **11** was efficiently achieved in ten steps in 44% overall yield from propynyl alcohol **1**[3] (Scheme 1).

1 was quantitatively silylated with *tert*-butyldimethylsilyl chloride (TBDMSCl). The lithium derivative of **2** was added to paraformaldehyde and then mesylated to yield **4** (74%). The quaternary centre was introduced by the deprotonation of methyl isobutyrate with LDA followed by its condensation on **4** to afford **5** in 96% yield. The ester was quantitatively reduced with $LiAlH_4$ and the corresponding alcohol **6** was subjected to a Swern oxidation (97%). One-carbon homologation of aldehyde **7** was next accomplished by a Corey–Fuchs reaction[4] to provide **9** in 65% yield which was converted to propynyl alcohol **10** (97%) by the fluoride anion. Finally, quantitative silylation of **10** with bromomethyldimethylsilyl chloride afforded **11**.

We subjected propynyl ether **11** to the conditions of radical cyclisation† in the presence of 10 equiv. of acrylonitrile followed by a treatment with methyllithium.[5] Unfortunately, this led to a complex mixture of unidentified products. To understand this problem, **11** was cyclised in the absence of acrylonitrile in order to verify the compatibility of the terminal acetylenic function (Scheme 2).

This one-pot reaction allowed the synthesis of a functionalised hydrindene framework of great interest.[6] **13** was isolated as a single stereoisomer in a modest yield‡ (35%). Two consecutive 5-*exo* type cyclisations[7] afforded the regio- and stereo-selective formation of a homoallyl radical intermediate **12**. This 1,3-diastereoselective induction was the result of a chairlike transition state during the cyclisation of the vinyl radical.[2] Then, the radical intermediate **12** cyclised *via* a 6-*exo-dig* process instead of being reduced. This seems to be favored by a Thorpe–Ingold effect of the *gem*-dimethyl group.[8]

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Footnotes

† A benzene solution (10 ml) of Bu_3SnH (1.65 mmol) containing AIBN (0.15 mmol) was added by a syringe pump over a period of 8 h to a solution of **11** (1.5 mmol) and acrylonitrile (15 mmol) in refluxing benzene (60 ml) under argon. After completion of the addition, the mixture was allowed to reflux for 5 additional hours and cooled at 0 °C. Methyllithium (2 mmol) was then added and the mixture was stirred for 1 h under argon. The organic phase was washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography (silica).

‡ The reaction has not been optimised. Nevertheless, further investigations using the treatment with methyllithium is under progress in our laboratory in view of the synthesis of variously substituted trimethylenemethane (TMM) precursors as reagents for the [3 + 2] cycloaddition reactions (B. M. Trost, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 1).

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