Pergamon

Tetrahedron, Vol. 53, No. 40, pp. 13797-13810, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00899-5

Design of a Radical Translocation Step through 1, n (n = 5, 6, 7) Hydrogen Transfers for Incorporation into New Radical Cascades

Alexandre Gross, Louis Fensterbank, Stéphane Bogen, René Thouvenot# and Max Malacria*

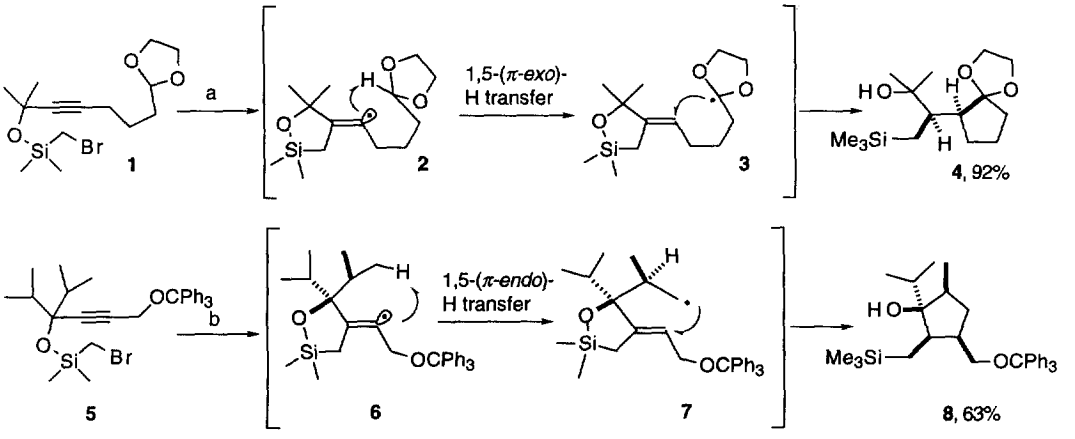
Université P. et M. Curie, Laboratoire de Chimie Organique de Synthèse, associé au CNRS, Tour 44-54, B. 229, 4, place Jussieu 75252 PARIS Cedex, France.

#Université P. et M. Curie, Laboratoire de Chimie des Métaux de Transition, associé au CNRS, Bâtiment F, B. 42, 4, place Jussieu, 75252 PARIS Cedex, France.

Abstract : The scope and limitations in the 1,n (n = 5, 6, 7) hydrogen transfers from homoallyl radicals of type **10** have been delineated. Encouraging results have notably been obtained with a dioxolane on the side chain to promote a 1,6-H transfer and with a TBS ether to promote a 1,5-H transfer.

Introduction

The vinyl radical generated from the highly efficient and regioselective 5-*exo-dig* cyclization[1] of bromomethyldimethylsilyl propargyl ethers has revealed as a very versatile synthetic tool.[2,3] We have illustrated recently its high reactivity towards hydrogen transfers, leading for instance to translocated radicals **3**[4] and **7**[5] from vinyl radicals **2** and **6** respectively. A further 5-*exo-trig* cyclization or a more unusual 5-*endo-trig* cyclization can afford cyclopentane derivatives **4** and **8** in a completely diastereoselective manner.



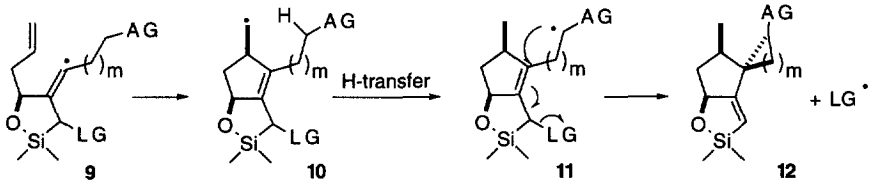
a :1. TMS_3SiH, 2. MeLi; b : 1. Bu_3SnH, 2. MeLi.

Scheme 1

The vinyl radical generated from the 5-*exo-dig* cyclization of bromomethyldimethylsilyl propargyl ethers is also an efficient trigger for radical cascades based on cyclizations.[2] Thus, when an allyl group is present at the propargylic position, vinyl radical of type **9** readily engages in a 5-*exo-trig* cyclization to form **10**.[3] A crucial feature of this cyclization is the complete diastereoselectivity of the carbon-carbon bond formation, placing the

E mail : malacria@ccr.jussieu.fr, Fax : 33 01 44 27 73 60

radical *syn* to the carbon-oxygen bond. Numerous applications directed towards the stereoselective synthesis of functionalized carbocycles (hydrindenes, steroids) have therefore been developed.[3,6] A potentially new application of homoallyl radical **10**, as a trigger for radical translocations through hydrogen transfers, is also conceivable. Activating groups (AG) would direct a hydrogen transfer in 1,5, 1,6 or 1,7 positions on the external alkyl chain. Subsequent 3-, 4-*exo-trig* cyclizations driven by the β-elimination of a radical leaving group (LG), or a 5-*exo-trig* cyclization, would provide an access to interesting spiro systems. Herein, we have examined the scope and the limitations of the translocation step from homoallyl radicals **10**.



Scheme 2

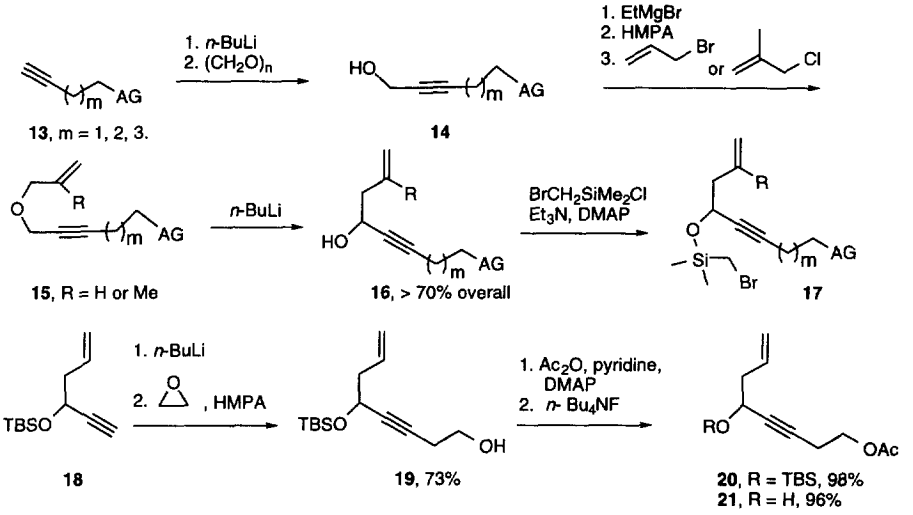
Oxygen and nitrogen centered radicals are very prone to 1,5-hydrogen transfers as established by the versatility of the Barton-Heusler[7] reaction and of the Hofman-Löffler-Freytag[8] reaction respectively.[9] Highly reactive carbon centered radicals (vinyl and aryl) have also been used to provide useful radical translocations.[10] Curran has notably defined the concept of Protection and Radical Translocation (PRT) groups such as 2-*O*-(2-bromoaryl)dimethylsilyl ethers, arylamides and 2-bromo-4-methoxyphenyl ether, which, thanks to their dual role, have served in numerous synthetic applications.[11] Moreover, on using a fruitful model, Curran was also able to propose a ranking of activating groups in the 1,5-hydrogen transfers of vinyl radicals.[12] However, much less is known about hydrogen transfers involving two less reactive saturated carbon sites. Lefort[13] has shown that a primary radical of a long alkyl chain migrates principally in a 1,5- and a 1,6-manner and that the 1,5/1,6 migration ratio is close to 3.3. Minor amounts of 1,10- and 1,11-H transfers were also detected. Very recently, Masnyk[14] has reported some similar results in the radical rearrangement of α-iodoalkylphenylsulfones. Besides a few incidental examples,[15] and to the best of our knowledge, only two groups have studied on a systematic basis hydrogen transfers involving two saturated carbon sites in cyclic series. De Mesmaeker[16] has examined the C(5)-epimerization in glycopyranosides during the cyclization of anomeric radicals and Crich[17] has devised a 1,5-hydrogen transfer from a methyl radical to the anomeric center which serves for the inversion of α- to β-mannopyranosides.

Interestingly, all reports of hydrogen transfers unify in a certain sense and suggest that the radical translocation originates from a balance of the C-H bond dissociation energy, the proximity of the reacting centers and the transition state geometry. Theoretical studies by Dannenberg[18] show that activation enthalpies for 1,5- and 1,6-H transfers are the lowest due to C-H-C angles only slightly distorted from linearity in the transition state. Particularly favorable C-H-C angles are also involved in 1,7- and 1,8-H transfers, but conformational strain renders these transfers much less available. In the case of 1,3- and 1,4-H transfers, C-H-C angles are too distorted from linearity and these transfers are quite rare.[19] Moreover, Houk[20] has estimated that the entropic advantage of forming a six-membered ring over a seven-membered ring is sufficient to overcome the more favorable enthalpy of the 1,6-H transfer, thus justifying the generally observed preponderance of the 1,5-H transfer over the 1,6-H transfer.

Results and Discussion

1. Preparations of Precursors

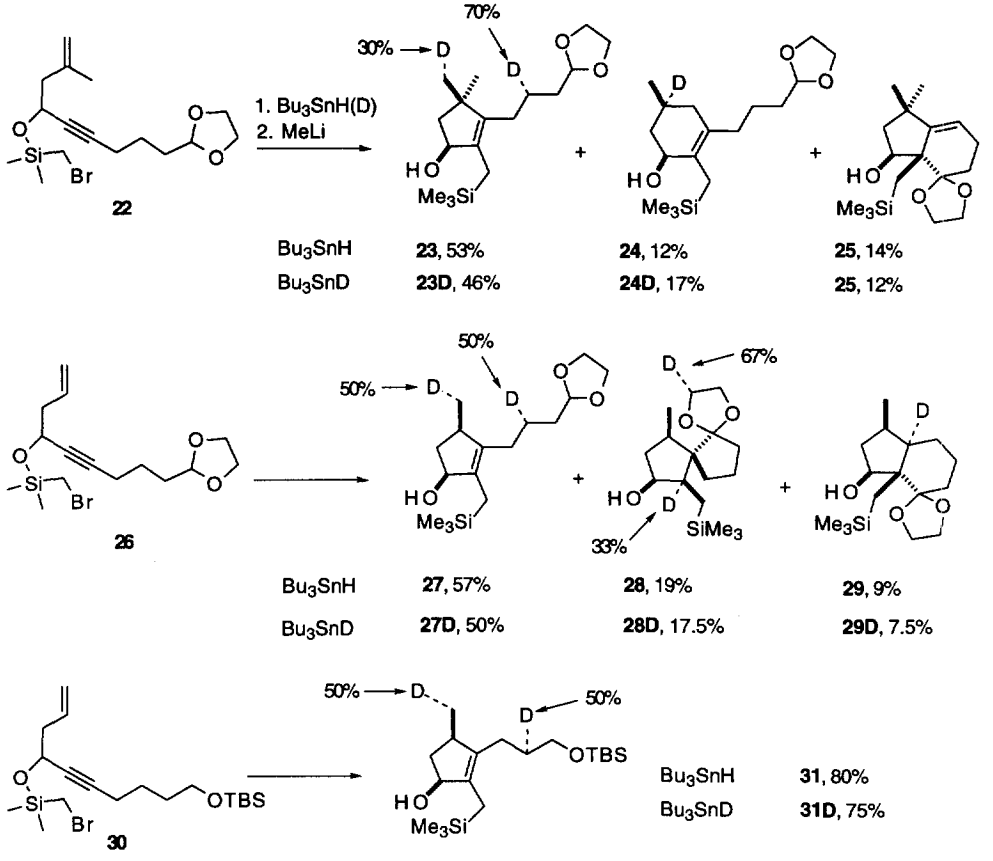
The preparation of precursors relies on chemistry we have already published[3] and is summarized in Scheme 3. The succession of the alkylation of an acetylenic precursor **13** with paraformaldehyde in THF, etherification and [2,3]-Wittig rearrangement affords enynols **16** in overall satisfactory yields (> 70%). In most cases, the three reactions can be consolidated into a single step. Alcohols **16** were characterized as their silyl ethers **17** (see Experimental Section). Silylether **18** was obtained from the corresponding previously reported alcohol.[3] Homologation by two carbons using ethylene oxide[21] gave alcohol **19**. Enynol **21** was then obtained in high yield through an acetylation and a desilylation.



Scheme 3

2. 1,7-hydrogen transfers

Recently, we have reported the chemoselectivity of the vinyl radical of type **9** (m = 3) towards a 5-*exo-trig* cyclization process rather than a 1,5-hydrogen transfer (as in **2** -> **3**) and studied the behavior of **22**, **26** and **30** in radical reaction conditions.[6] Reexamination of these reactions with Bu_3SnD in the same reaction conditions (see Experimental Section) has shed new light on our results (Scheme 4). In addition to the two previously reported products **23** and **24**, we found that cyclization of **22** also afforded hydrindene **25**. This product would originate from a 1,7-H transfer involving the homoallyl radical **9** and the dioxolane moiety and a subsequent 6-*endo-trig* cyclization in the convex face of the molecule. No 5-*exo-trig* cyclization would be possible here due to the presence of the *gem*-dimethyl group, adjacent to the double bond. The *gem*-dimethyl group would also prevent a final stannane reduction to occur and a rare β-hydrogen abstraction presumably takes place.[5] Two sites of deuteration were observed on **23D** which indicated a large amount of 1,5-H transfer on the alkyl chain. No deuterium is present on the dioxolane suggesting that any 1,7-H transfer occurring gives birth to bicyclic derivative **25**. Cyclohexene **24** might originate from a direct 6-*endo-trig* cyclization and/or from the rearrangement of an α-cyclopropyl radical as proposed by Beckwith and Stork.[22] Its stereochemistry is proposed by analogy with previous findings in this laboratory.[3]



Scheme 4

In addition to cyclopentene **27**, the cyclization of **26** provided a 70:30 mixture of bicyclic derivatives **28** and **29**. We reasoned that the minor product **29** is not a diastereomer of the 5-*exo-trig* cyclization of the dioxolanyl radical (generated from the 1,7-H transfer) but more likely the 6-*endo-trig* regioisomer. In this case, the final stannane reduction *anti* to the methyl would be possible affording **29** as the sole diastereomer. Regioisomers **28** and **29** are inseparable. The deuterium NMR spectrum of the mixture indicates three resonances (**28D** δ 3.85 (0.5D), 1.95 (0.2D), **29D** δ 1.53 (0.3D)). The deshielded resonance suggests that deuterium was incorporated on the dioxolane ring. Correlation of this with the proton, carbon and 2D NMR spectra of this mixture unambiguously revealed that the β-silyl radical resulting from the 5-*exo-trig* cyclization of the dioxolanyl radical (leading to major component **28** or **28D**) undergoes in approximately 67% efficiency an additional 1,5-H transfer from the dioxolane moiety. This hydrogen transfer is only possible if the dioxolane is present on the α-face of the molecule, implying that the 5-*exo-trig* cyclization proceeds completely *anti* to the methyl group.

1,7-H translocations are relatively rare[23] and have never been reported in the case of an alkyl to alkyl radical migration. De Mesmaeker was able to obtain high yields of 1,7-H transfers from aryl radicals on conformationally restricted amides but in some cases, 1,5-H transfers could be highly competitive. We also observe a severe competition from 1,5-H transfers (Table 1) in every case. Interestingly, cyclization of **30** with Bu3SnD

confirmed that no 1,7-H transfer occurs. No bicyclic product was isolated and no deuterium was incorporated on the CH_2OTBS moiety. The occurrence of 1,7-H transfers with **22** suggests that an eight-membered transition state with the alignment of the C-H bond and the 2p orbital of the radical takes place on the β-face (**22->25**). The more bulky TBS group might not be suitable for this approach from the concave face. This failure of a OTBS group to promote a hydrogen transfer also marks a contrast with Curran's observation[12] that a OTBS group is a much better activating group for a 1,5-H transfer from a vinyl radical than a dioxolane.

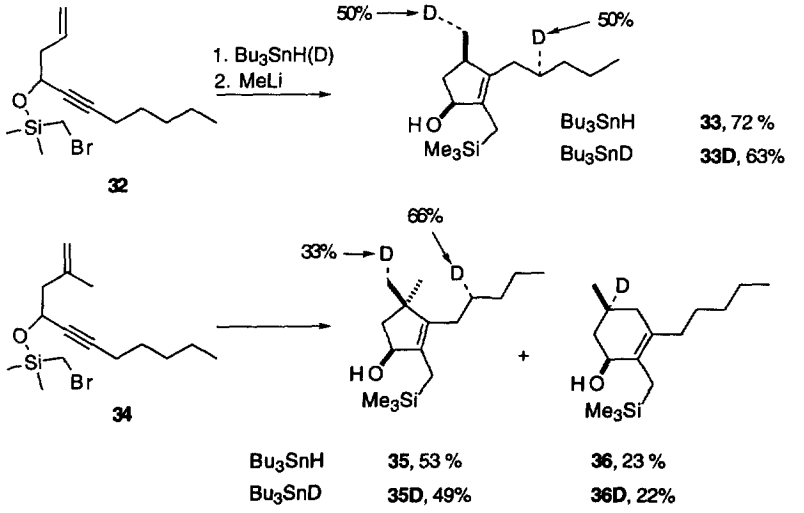
precursor	intermolecular reduction[a]	1,5-H transfer[b]	1,7-H transfer
22	41%[c]	43%	16%
26	33%	33%	33%
30	50%	50%	0%

[a] Intermolecular reduction refers to stannane reduction of the homoallylic position.
[b] Broad resonances in the ^2H NMR spectrum may include minor amounts of 1,6-H transfers.
[c] The amount of cyclohexene **24** is included.

Table 1

3. blank experiments

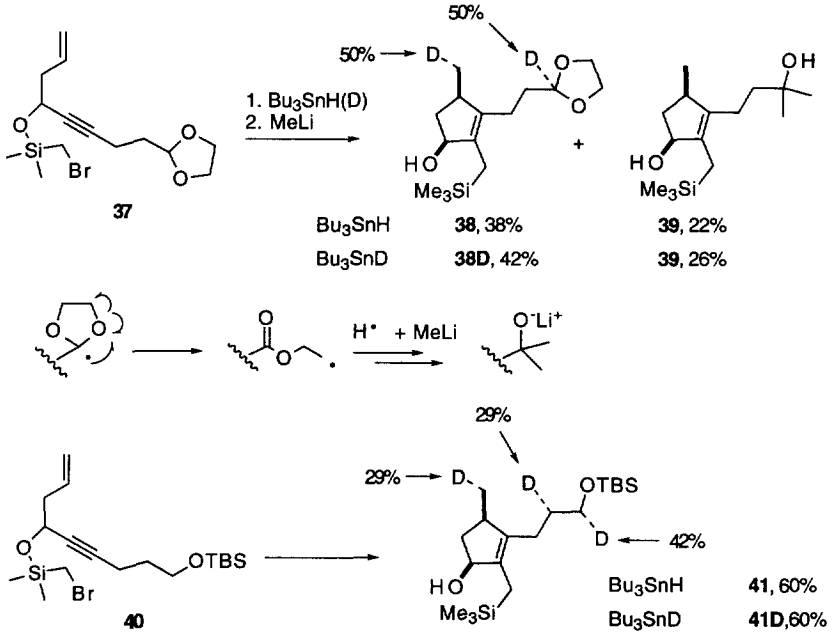
Intrigued by the large amount of 1,5-H transfer on the alkyl chain, we wanted to investigate the behavior of precursors bearing no activating group. Treatment of **32** and **34** with Bu_3SnD in identical reaction conditions confirmed the previous results and showed large amount of 1,5-H transfers. Due to broad resonances in the deuterium NMR spectrum, minor amounts of 1,6-H or 1,7-H transfer cannot be excluded. However in both cases, the carbon NMR spectrum shows a triplet 1/1/1 for the carbon of the 1,5 migration, suggesting prominent deuterium incorporation at this position. Fully consistent with the inefficient activation of a OTBS moiety at the 1,7 position, precursors **30** and **32** yield the same partition (1:1) between stannane reduction at the homoallylic position and 1,5-H transfer. This would correspond to the background level.



Scheme 5

4. 1,6-hydrogen transfers

Our next goal was to design a precursor which could overcome the 1,5-H transfer and selectively give some 1,6-H transfer on the alkyl chain. We therefore prepared **37** and **40** and assessed their ability to meet our requirements (Scheme 6). The cyclization of the dioxolane derivative **37** furnished two products, the expected cyclopentene **38** and diol **39**, whose structure was determined through usual NMR techniques. Diol **39** probably originates from the fragmentation of the dioxolane moiety, which furnishes an ester. Excess methyllithium smoothly adds to the ester and provides the *gem*-dimethyl functionality of diol **39**. This fragmentation pathway is precedented[24] and has been for instance described in the radical rearrangement of 2-methoxytetrahydropyran to methyl valerate.[25] In our case, it suggests that a 1,6 migration occurred generating a dioxolanyl radical. This radical can undergo a reversible 4-*exo-trig* cyclization, fragment or be reduced. Only the last two pathways have been observed and the fragmentation is thus a direct measurement of the 1,6-H transfer.



Scheme 6

Interestingly, the deuterium NMR of cylopentene **38D** shows two resonances (δ= 4.82 (0.5D), 1.03 (0.5D)). No 1,5-H transfer is observed. In comparison, the OTBS ether proves much less efficient for directing the 1,6-H transfer, since a mixture of 1,5 and 1,6 migrations is observed on **41D** (Table 2).

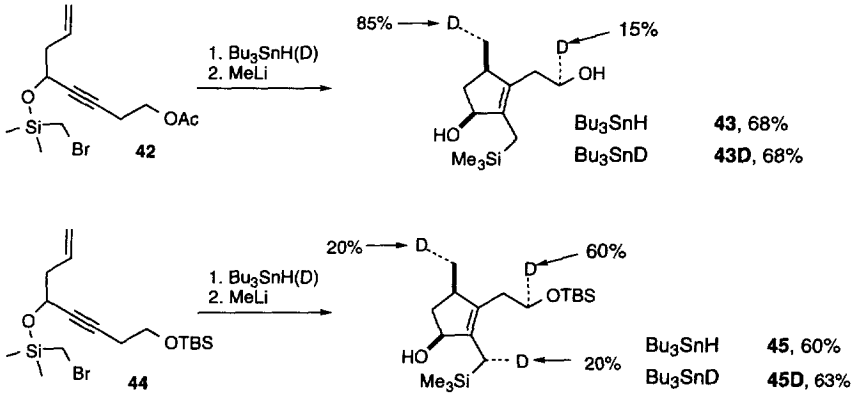
precursor	intermolecular reduction[a]	1,5-H transfer	1,6-H transfer
37	31%	0%	69%
40	29%	29%	42%

[a] Intermolecular reduction refers to stannane reduction of the homoallylic position.

Table 2

5. 1,5-hydrogen transfer

We know from this study that homoallyl radicals of type **10** migrate in a 1,5-manner on an unactivated alkyl chain to an extent of 50%. We wanted to pursue this study in order to find an activating group which could ensure a high yielding 1,5 translocation. Due to the fragility of the butynal dioxolane array in many synthetic endeavors and its potentially troublesome radical fragmentation, we focused on monooxygenated substituents at the 1,5 position. We notably investigated the performance of an acetate group as an activating group (precursor **42**), which, to our knowledge, has never been examined before in hydrogen transfer studies. We were, therefore, very surprised to observe that only 15% of 1,5-H transfer occurred. This is less than with a plain alkyl chain! No 1,8-H transfer from the methyl of the acetate group could have taken place since the mass spectrum of **43D** indicates a deuterium incorporation > 90%. This surprising result could be in part justified by the low efficiency of an acetate group to stabilize radicals.[26] An acetate could therefore be an interesting hydroxy protecting group, whenever low radical activation is required. More promising results were obtained with a TBS ether, since only 20% of stannane reduction took place at the homoallylic position. A deuterium resonance at (δ = 1.53, (0.20D)) also shows some incorporation on the α-silyl methylene. This probably originates from a double 1,5-H transfer. Previous work in our laboratory has indeed established the high reactivity of this α-silyl methylene towards hydrogen transfers.[5] In our case, the bulky OTBS group might slow down the intermolecular reduction, and favor a new hydrogen transfer. Total amount of 1,5-H transfer therefore rises to 80%.



Scheme 7

Conclusion

The above results give some insights into the scope and limitations of a few activating groups for conducting a radical translocation between two saturated sites in cyclic series. Indeed, it was found that homoallyl radicals of type **10** translocate onto an unactivated alkyl side chain primarily in a 1,5 manner and to the extent of 50%. A dioxolane group directs selectively a 1,6-H transfer in 70% efficiency, whereas a OTBS moiety results in 80% of 1,5-H transfer. Interestingly, negative activation is observed with an acetate in the 1,5 position, reducing the 1,5-H transfer to 15%. Further work will focus on the development of the 3- and 4-*exo-trig* cyclizations, resulting from the 1,5- and 1,6-H transfers described herein.

Experimental Section

^{1}H-NMR and ^{13}C-NMR spectra were recorded at room temperature, either at 400 MHz and 100 MHz respectively on an ARX 400 Bruker spectrometer or at 200 MHz and 50 MHz respectively on an AC200 Bruker spectrometer. ^{2}H (deuterium) NMR spectra were obtained at room temperature at 46 MHz on an AC300 spectrometer with multinuclear capacity. For internal referencing deuterated chloroform (2.5% in volume : δ ^{2}H = 7.27 ppm) was added to the $CHCl_3$ solution in 5 mm o. d. tubes. The spectra were recorded without lock through the lock coil of a QNP probehead. Infrared (IR) spectra were recorded with a Perkin Elmer 1420 spectrometer. Mass spectra (MS) were obtained on a GC-MS Hewlett-Packard HP 5971 apparatus and on a NERMAG R-30-10 apparatus. Melting points were obtained on a Reichert apparatus and are uncorrected. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F 254. Silica gel Merck Geduran SI (40-63 µm) was used for column chromatography using Still's method.[27]

Solvents : Ethyl ether and THF were distilled from sodium-benzophenone ketyl. Benzene, dichloromethane and triethylamine were distilled from calcium hydride. HMPA was distilled under reduced pressure after drying over CaH_2. Chromatography solvents : EE refers to ethyl ether, PE refers to petroleum ether.

Reagents : Starting alkynes **13** (2-but-3-ynyl-[1,3]dioxolane,[28] *tert*-butyldimethyl-pent-4-ynyloxy-silane,[29] *tert*-butyldimethyl-but-3-ynyloxy-silane[30]) have been prepared according to literature procedures.

Paraformaldehyde was dried using an azeotropic distillation with benzene.

Tributyltin deuteride (isotopic purity > 95%) was purchased from Aldrich. All mass spectra of deuterated products indicated a deuterium incorporation > 95%.

1) General procedure for the synthesis of alcohols **16** :

To a solution of alkyne **13** (10 mmol, 1 equiv.) in THF (20 mL) at -78°C and under N_2 were added 4 mL (10 mmol, 1 equiv.) of *n*-BuLi (2.5 M in hexanes). After 10 min at -78°C, dried paraformaldehyde (1.5 g, 5 equiv.) was added in one portion to the reaction mixture. After 10 min at -78°C, the reaction mixture was warmed to rt and stirred for an additional 20 min period. The reaction was quenched with 50 mL of a saturated NH_4Cl solution and the aqueous layer extracted 4 times with 30 mL of ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give crude alcohol **14** (crude yield > 90%).

To a solution of crude alcohol **14** in THF (20 mL) and 5 mg of 1,10-phenanthroline was added a THF solution of EtMgBr at 0°C and under N_2, until a persistent red color appeared. To this mixture were added HMPA (4 equiv.) and the allyl halide (methallyl chloride or allyl bromide, 1.5 equiv.). The reaction mixture was then heated to reflux for a few hours. When all of the alcohol **14** was consumed (checked by TLC), the reaction mixture was diluted with 30 mL of ether. The organic layer was washed with a saturated NH_4Cl solution and brine, and dried over $MgSO_4$. After concentration *in vacuo*, the crude product was filtered over a short pad of silica gel (crude yield of propargylic ether **15** > 90%).

The allyl-propargylic ether **15** was dissolved into 15 mL of THF. After cooling down the reaction mixture to -78°C, 1 equiv. of *n*-BuLi (2.5 M in hexanes) was added. An instantaneous red-brown color appears. After warming to rt, the reaction mixture was diluted with 50 mL of ether. The organic layer was washed with a saturated NH_4Cl solution and brine, and dried over $MgSO_4$. After concentration *in vacuo*, the crude product was purified by flash chromatography, affording alcohols **16**. (overall yield from **12**, 70-80%). Alcohols **16** were fully characterized as silylethers **17**, prepared according to the following general procedure.

2) Preparation of bromomethyldimethylsilyl ethers :

To a mixture of the corresponding alcohol, triethylamine (1.5 equiv.) and a catalytic amount of 4-DMAP (10 mol %) in CH_2Cl_2, was added at 0°C *via* syringe bromomethyldimethylchlorosilane (0.9 - 1 equiv.). After

stirring at rt for 15 min, the reaction mixture was diluted with CH_2Cl_2, washed twice with a saturated solution of ammonium chloride, and twice with brine. After drying over $MgSO_4$, and concentrating *in vacuo*, the crude product was purified by flash chromatography, to afford as a colorless oil :

Silyl ethers **22**, **26**, **30**, **32** and **34** have been previously reported (see references 3 & 6 for spectral data).

5-bromomethyldimethylsilyloxy-1-[1,3]dioxan-2-yl-oct-7-en-3-yne (37). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.80 (ddt, *J*=17.2, 10.2, 7.1 Hz, 1H), 5.10 (m, 2H), 4.93 (t, *J*=4.6 Hz, 1H), 4.40 (m, 1H), 3.96 (m, 2H), 3.85 (m, 2H), 2.58-2.50 (mAB, 2H), 2.37 (m, 2H), 2.34 (td, *J*=7.6, 1.5 Hz, 2H), 1.85 (td, *J*=7.6, 4.6 Hz, 2H), 0.31 (s, 3H), 0.30 (s, 3H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 133.8, 117.8, 103.2, 85.0, 80.9, 65.0, 63.3, 43.2, 32.9, 16.0, 13.6, -2.4, -2.6; Anal. Calcd. for $C_{14}H_{23}O_3SiBr$: C, 48.42, H, 6.67. Found : C, 48.56, H, 6.91.

5-bromomethyldimethylsilyloxy-1-*tert*-butyldimethylsilyloxy-non-8-en-4-yne (40). ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 5.85 (m, 1H), 5.12 (m, 2H), 4.40 (tt, *J*=6.5, 2.0 Hz, 1H), 3.65 (t, *J*=6.0 Hz, 2H), 2.55-2.47 (mAB, 2H), 2.38 (q, *J*=6.5 Hz, 2H), 2.26 (td, *J*=7.0, 2 Hz, 2H), 1.64 (m, 2H), 0.87 (s, 9H), 0.29 (s, 6H), 0.04 (s, 6H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 133.9, 117.8, 85.7, 81.7, 63.4, 61.6, 43.3, 31.7, 26.0, 18.4, 16.4, 15.1, -2.4, -2.5, -5.2; IR (neat) 3060, 2940, 2840, 2210, 1640, 1470, 1250, 1100, 840 cm^{-1}. Anal. Calcd. for $C_{18}H_{35}O_2Si_2Br$: C, 51.53, H, 8.40. Found : C, 51.69, H, 8.41.

5-bromomethyldimethylsilyloxy-1-*tert*-butyldimethylsilyloxy-oct-7-en-3-yne (44). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.65 (ddt, *J*=17.2, 10.1, 7.1 Hz, 1H), 5.05 (m, 2H), 4.34 (tt, *J*=6.6, 2.0 Hz, 1H), 3.72 (t, *J*=7.2 Hz, 2H), 2.59-2.52 (mAB, 2H), 2.42 (m, 4H), 0.86 (s, 9H), 0.32 (s, 6H), 0.10 (s, 6H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 133.6, 117.6, 82.8, 81.5, 63.1, 61.6, 43.0, 25.7, 23.0, 18.2, 16.1, -3.0, -5.4; IR (neat) 3080, 2960, 2860, 2220, 1640, 1460, 1250, 110, 860 cm^{-1}.

Preparation of silylether **42** :

3-*tert*-butyldimethylsilyloxy-hex-5-en-1-yne (18). To a mixture of hex-5-en-1-yn-3-ol[3] (3.45 g, 36 mmol, 1 equiv.), triethylamine (7.50 mL, 54 mmol, 1.5 equiv.) and 4-DMAP (0.44 g, 3.6 mmol, 0.1 equiv.) in CH_2Cl_2 (60 mL) was added *t*-butyldimethylchlorosilane (5.4 g, 36 mmol, 1 equiv.). The reaction mixture was stirred for 48 h at rt, and then diluted with 120 mL of ether. The organic layer was then washed with a saturated NH_4Cl solution and brine, and dried over $MgSO_4$. After concentration *in vacuo*, the crude product was purified by flash chromatography (PE:EE, 95:5) affording 6.32 g (83%) of **18** as a pure oil : ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.71 (ddt, *J*=16.8, 10.2, 6.6 Hz, 1H), 4.98 (m, 2H), 4.23 (td, *J*=6.6, 2.0 Hz, 1H), 2.30 (m, 3H), 0.77 (m, 9H), 0.01 (s, 3H), -0.01 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 136.5, 119.7, 86.0, 77.0, 65.7, 45.7, 27.3, 19.1, −3.7, −3.9; IR (neat) 3300, 3060, 2940, 2840, 2140, 1640, 1460, 1250, 1080, 830 cm^{-1}.

5-*tert*-butyldimethylsilyloxy-oct-7-en-3-yn-1-ol (19). To a solution of **18** (2.10 g, 10 mmol, 1 equiv.) and HMPA (0.52 mL, 3 mmol, 0.3 equiv.) in a 20 mL ether: THF (3:1) mixture was added 3.90 mL (9.8 mmol, 0.98 eq) of a 2.5 M solution of *n*-BuLi at -40°C.[21] The solution was stirred for 15 min, and then neat ethylene oxide (2 mL, 20 mmol, 2 equiv.) was added. The reaction mixture was stirred at rt for 46 h. Ether was added and the organic layer was washed with a saturated NH_4Cl solution and brine, and dried over $MgSO_4$. After concentration *in vacuo*, the crude product was purified by flash chromatography (PE:EE, 60:40) affording 1.85 g (73%) of alcohols **19** as a pure oil : ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 5.84 (ddt, *J*=17.3, 10.7, 6.6 Hz, 1H), 5.12 (m, 2H), 4.40 (m, 1H), 3.71 (q, *J*=6.6 Hz, 2H), 2.50 (td, *J*=6.6, 2.0 Hz, 2H), 2.43 (t, *J*=6.6 Hz, 2H), 0.92

(m, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 134.6, 117.9, 84.0, 81.7, 63.3, 61.4, 43.8, 26.2, 23.5, 18.7, -4.1, -4.6; IR (neat) 3350, 3060, 2920, 2840, 2210, 1640, 1470, 1250, 1080 cm^{-1}.

5-*tert*-butyldimethylsilyloxy-oct-7-en-3-ynyl-acetate (20). To a solution of alcohol **19** (1.85 g, 7.3 mmol, 1 equiv.) and 4-DMAP (89 mg, 0.73 mmol, 0.1 equiv.) in 20 mL of pyridine was added at 0°C acetic anhydride (1.72 mL, 18.25 mmol, 2.5 equiv.). After 20 min at 0°C, the reaction mixture was stirred at rt for an additional 30 min period. Ether was added and the organic layer was washed with a saturated NH_4Cl solution and brine, and dried over $MgSO_4$. After concentration *in vacuo*, the crude product was purified by flash chromatography (PE:EE, 80:20) affording 2.11 g (98%) of acetate **20**. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.84 (ddt, *J*=17.2, 10.2, 7.1 Hz, 1H), 5.10 (m, 2H), 4.34 (tt, *J*=6.6, 2.0 Hz, 1H), 4.15 (t, *J*=6.6 Hz, 2H), 2.55 (td, *J*=6.6, 2.0 Hz, 2H), 2.42 (t, *J*=6.6 Hz, 2H), 2.08 (s, 3H), 0.90 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 171.2; 134.5, 117.9, 83.4, 80.7, 63.3, 62.8, 43.7, 26.2, 21.2, 19.6, 18.7, -4.13, -4.61. IR (neat) 3050, 2980, 1740, 1640, 1230, 1080 cm^{-1}. Anal. Calcd. for $C_{16}H_{28}O_3Si$: C, 64.81, H, 9.51. Found : C, 64.93, H, 9.51.

5-hydroxy-oct-7-en-3-ynyl-acetate (21). Acetate **20** (2.11g, 7.13 mmol) was dissolved into 10 mL of THF. At 0°C, 8.5 mL (8.5 mmol, 1.2 equiv.) of a 1.0 M solution of *n*-Bu4NF in THF were added. After stirring for 10 min at rt, 20 mL of ether were added. The organic layer was washed with brine, and dried over $MgSO_4$. After concentration *in vacuo*, the crude product was purified by flash chromatography (PE:EE, 70:30) affording 1.24 g (96%) of alcohol **21**. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.87 (ddt, *J*=17.3, 10.7, 7.1 Hz, 1H), 5.16 (m, 2H), 4.40 (m, 1H), 4.15 (t, *J*=7.1 Hz, 2H), 2.57 (td, *J*=7.1, 2.0 Hz, 2H), 2.45 (t, *J*=7.1 Hz, 2H), 2.07 (s, 3H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 171.3, 133.5, 119.3, 82.6, 81.6, 62.6, 62.0, 42.7, 21.3, 19.6; IR (neat) 3400, 3060, 2980, 2900, 1740, 1640, 1230, 1030 cm^{-1}. Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91, H, 7.74. Found : C, 65.82, H, 7.78.

5-bromomethyldimethylsilyloxy-oct-7-en-3-ynyl-acetate (42). To a mixture of alcohol **21** (1.24 g, 6.82 mmol, 1 equiv.), 4-DMAP (83 mg, 0.68 mmol, 0.1 equiv.) and triethylamine (1.42 mL, 10.23 mmol, 1.5 equiv.) in CH_2Cl_2 (14 mL), was added at 0°C bromomethyldimethylchlorosilane (0.87 mL, 6.48 mmol, 0.95 equiv.). After stirring for 1.5 h at rt, the reaction mixture was diluted with CH_2Cl_2, washed twice with a saturated NH_4Cl solution and brine, and dried over $MgSO_4$. After concentration *in vacuo*, the crude product was purified by flash chromatography (PE:EE, 85:15) affording 1.70 g (79%) of silylether **42**. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.84 (ddt, *J*=17.2, 10.3, 6.8 Hz, 1H), 5.12 (m, 2H), 4.40 (tt, *J*=6.5, 1.8 Hz, 1H), 4.15 (t, =6.8 Hz, 2H), 2.55 (m, 4H), 2.43 (t, *J*=6.8 Hz, 2H), 2.08 (s, 3H), 0.33 (s, 3H), 0.32 (s, 3H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 171.3, 134.2, 118.2, 82.9, 82.2, 67.5, 66.9, 47.6, 25.6, 23.8, 20.9, -1.8, -2.0; IR (neat) 3030, 2950, 2220, 1735, 1635, 1430, 1230, 1080, 900 cm^{-1}. Anal. Calcd. for $C_{13}H_{21}O_3SiBr$: C, 46.85, H, 6.34. Found : C, 46.97, H, 6.38.

3) General procedure for the radical cyclization of the bromomethyldimethylsilyl ethers (**22**, **26**, **30**, **32**, **34**, **37**, **40**, **42**, **44**) :

To a refluxing benzene solution, under nitrogen, of the bromomethyldimethylsilyl ether (1 mmol) in 40 mL of benzene, and 8 mg of AIBN (5 mol %) was added a 13.5 mL benzene solution of tributyltin hydride or tributyltin deuteride (360 µL, 1.30 mmol) and AIBN (15 mol %) *via* a syringe-pump (2.10^{-4} $mol.h^{-1}$). After completion of the reaction, the mixture was allowed to reflux for 2 additional hours. Five equivalents of methyllithium in ether were then added at 0°C and the mixture was stirred for 30 min at rt. After quenching with a

saturated solution of ammonium chloride, and extracting with ether, the organic phase was then washed with brine and dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was then purified by flash chromatography with a solvent mixture.

Radical cyclization of **22** :

See the general procedure above on a 1 mmol scale. Chromatography (PE:EtOAc, 70:30) afforded :

3-(3-[1,3]dioxan-2-ylpropyl)-4,4-dimethyl-2-trimethylsilylmethylcyclopent-2-en-1-ol (23), see ref. 6.

23D, (144 mg, 46%) ^{2}H-NMR ($CHCl_3$+ 2.5% $CDCl_3$, 46 MHz) δ 1.50 (0.7D), 1.09 (0.3D); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 24.2 (residual), 23.8 (t, *J*=19 Hz, CHD); IR (neat) 3400, 2940, 2880, 2150, 1650, 1400, 1250, 1080 cm^{-1}. GC/CIMS *m/z* : 331 (MNH_4^+, 4), 296 (MH^+-H_2O, 100).

3-(3-[1,3]dioxan-2-ylpropyl)-5-methyl-2-trimethylsilylmethylcyclohex-2-en-1-ol (24), see ref 6.

24D, (53 mg, 17%) ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.90 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.6 (t, *J*=19 Hz, CD); IR (neat) 3400, 2960, 2120, 2150, 1450, 1400, 1270, 840 cm^{-1}. GC/CIMS *m/z* : 331 (MNH_4^+, 40), 296 (MH^+-H_2O, 100).

7,7-dimethyl-9-hydroxy-1-trimethylsilylmethylspiro[bicyclo[4,3,0]non-5-ene-2,2'-perhydro [1,3] dioxolane] (25). (38 mg, 12%), solid m.p. : 94-96°C, ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.29 (t, *J*=3.6 Hz, 1H), 4.45 (dd, *J*=10.3, 8.0 Hz, 1H), 4.09-3.93 (m, 4H), 2.25-2.22 (2H, m), 1.88-1.62 (m, 4 H), 1.29 (d, *J*=15.2 Hz, 1H), 1.22 (s, 3H), 1.06 (s, 3H), 0.73 (d, *J*=15.2 Hz, 1H), 0.1 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 155.6, 115.7, 112.2, 71.8, 64.9, 64.1, 54.0, 45.4, 37.3, 32.2, 31.7, 26.7, 24.6, 23.0, 1.5; IR (neat) 3350, 2940, 1650, 1450, 1240, 1160 cm^{-1}. GC/CIMS *m/z* : 328 (MNH_4^+, 27), 311 (MH^+, 100).

Radical cyclization of **26** :

See the general procedure above on a 1 mmol scale. Chromatography (PE:EtOAc, 80:20) afforded :

3-(3-[1,3]dioxan-2-yl-propyl)-4-methyl-2-trimethylsilylmethylcyclopent-2-en-1-ol (27), see ref 6.

27D, (147 mg, 50%) ^{2}H-NMR ($CHCl_3$+ 2.5% $CDCl_3$, 46 MHz) δ 1.55-1.35 (0.5D), 1.02 (0.5D).

3-hydoxy-5-methyl-2-trimethylsilylmethyldispiro[cyclopentane-1,1'-cyclopentane-2-2''-perhydro [1,3]dioxolane (28) and **3'-hydroxy-1'methyl-3a'-trimethylsilylmethylspiro [perhydro [1,3]dioxolane-2,4'-perhydroindene] (29)**, see ref. 6.

28D + 29D, (70:30, 75 mg, 25%) ^{2}H-NMR ($CHCl_3$+ 2.5% $CDCl_3$, 46 MHz) **28D** δ 3.85 (0.5D), 1.95 (0.2D), **29D** δ 1.53 (0.3D); ^{13}C-NMR ($CDCl_3$, 100 MHz) **28D** δ 64.8 (residual), 64.5 (t, *J*=22 Hz, CHD), 46.2 (residual), 46.0 (t, *J*=20 Hz, CD) **29D** δ 54.2 (t, *J*=22 Hz, CD); IR (neat) 3500, 2940, 1240, 1130 cm^{-1}. CIMS *m/z* : 300 (MH^+, 100).

Radical cyclization of **30** :

See the general procedure above on a 1 mmol scale. Chromatography (PE:EE, 80:20) afforded :

3-(4-tert-butyldimethylsilyloxybutyl)-4-methyl-2-trimethylsilylmethyl-2-cyclopenten-1-ol (31), see ref. 6.

31D, (278 mg, 75%) ^{2}H-NMR ($CHCl_3$+ 2.5% $CDCl_3$, 46 MHz) δ 1.70-1.30 (0.5D), 1.07 (0.5D); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 23.3 (residual), 23.1 (t, *J*=20 Hz, CHD), 19.8 (residual), 19.5 (t, *J*=20 Hz, CH_2D); IR (neat) 3350, 2940, 2920, 2850, 1460, 1250, 1100 cm^{-1}. CIMS *m/z* : 354 (MH^+-H_2O, 100).

Radical cyclization of **32** :

See the general procedure above on a 1 mmol scale. Chromatography (PE:EE, 85:15) afforded :

3-(pentyl)-4-methyl-2-trimethylsilylmethylcyclopent-2-en-1-ol (33), (183 mg, 72%) ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.42 (m, 1H), 2.55 (m, 1H), 2.48 (dt, *J*=13.2, 7.1 Hz, 1H), 2.10-1.90 (m, 2H), 1.62 (m, 2 H), 1.40-1.20 (m, 6H), 1.15 (dt, *J*=13.2, 5.1 Hz, 1H), 1.08 (d, *J*=6.6 Hz, 3H), 0.93 (t, *J*=6.7 Hz, 3H), -0.1 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 140.8, 135.0, 79.3, 42.0, 38.4, 32.5, 27.7, 26.9, 22.6, 20.8, 16.0, 14.1, -0.5; IR (neat) 3320, 2940, 2840, 1650, 1450, 1240, 1040 cm^{-1}. **33D**, (161 mg, 63%) ^{2}H-NMR ($CHCl_3$+ 2.5% $CDCl_3$, 46 MHz) δ 1.43-1.20 (0.5D), 1.05 (0.5D); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 27.8 (residual), 27.4 (t, *J*=19 Hz, CHD), 20.8 (residual), 20.5 (t, *J*=19 Hz, CH_2D); IR (neat) 3330, 2940, 2840, 2140, 1650, 1450, 1240, 1160, 1040, 850 cm^{-1}. CIMS *m/z* : 238 (MH^+-H_2O, 100).

Radical cyclization of **34** :

See the general procedure above on a 1 mmol scale. Chromatography (PE:EE, 90:10) afforded :

3-(pentyl)-4,4-dimethyl-2-trimethylsilylmethylcyclopent-2-en-1-ol (35), (142mg, 53%), ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.48 (t, *J*=6.1 Hz, 1H), 2.05 (dd, *J*=12.7, 7.1 Hz, 1H), 1.92 (m, 1H), 1.82 (m, 1H), 1.58-1.48 (mAB, 2H), 1.41 (dd, *J*=12.7, 5.1 Hz, 1H), 1.38-1.20 (m, 6H), 1.07 (s, 3H), 0.94 (s, 3H), 0.87 (t, *J*=6.7 Hz, 3H), 0.0 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 145.5, 136.0, 78.1, 51.8, 46.0, 34.1, 30.4, 29.7, 29.6, 26.9, 23.5, 17.2, 15.1, 0.5; IR (neat) 3340, 2940, 2850, 1650, 1460, 1250, 1160 cm^{-1}. Anal. Calcd. for $C_{16}H_{32}OSi$: C, 71.57, H, 12.01. Found : C, 71.49, H, 12.12. **35D**, (132 mg, 49%) ^{2}H-NMR ($CHCl_3$+ 2.5% $CDCl_3$, 46 MHz) δ 1.37 (0.66D), 1.07 (0.33D); IR (neat) 3340, 2940, 2860, 2410, 1450, 1250, 1160 cm^{-1}. CIMS *m/z* : 252 (MH^+-H_2O, 100).

3-(pentyl)-5-methyl-2-trimethylsilylmethylcyclohex-2-en-1-ol (36), (62 mg, 23%), ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.06 (m, 1H), 1.98 (m, 2H), 1.90 (d, *J*=16.4 Hz, 1H), 1.75 (m, 2H), 1.69 (m, 1H), 1.61-1.51 (m, 2H), 1.38-1.03 (m, 7H), 0.95 (d, *J*=6.6 Hz, 3H), 0.87 (t, *J*=6.7 Hz, 3H), 0.08 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 130.9, 130.7, 71.4, 42.5, 38.9, 34.3, 32.2, 29.1, 27.7, 22.8, 21.9, 17.6, 14.1, -0.2; IR (neat) 3340, 2940, 2860, 1450, 1245, 1040, 840 cm^{-1}. **36D**, (59 mg, 23%) ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.95 (s, 3H). ^{13}C-NMR (C_6D_6, 50 MHz) δ 27.4 (t, *J*=19 Hz, CD). IR (neat) 3360, 2940, 2850, 2140, 1450, 1245, 1040, 840 cm^{-1}. CIMS *m/z* : 252 (MH^+-H_2O, 100).

Radical cyclization of **37** :

See the general procedure above on a 1 mmol scale. Chromatography (PE:EE, 50:50) afforded :

3-(2-[1,3]dioxan-2-ylethyl)-4-methyl-2-trimethylsilylmethylcyclopent-2-en-1-ol (38), (110 mg, 38%) ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.83 (t, *J*=4.6 Hz, 1H), 4.43 (m, 1H), 3.93 (m, 2H), 3.83 (m, 2H), 2.52 (m, 1H), 2.42 (dt, *J*=12.8, 7.2 Hz, 1H), 2.14 (m, 1H), 2.04 (td, *J*=11.7, 4.6 Hz, 1H), 1.75 (m, 1 H), 1.60-1.50 (m, 3H), 1.15 (dt, *J*=12.8, 5.2 Hz, 1H), 1.04 (d, *J*=6.8 Hz, 3H), 0.05 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 138.8, 136.1, 104.2, 79.1, 64.95(2C), 42.1, 38.4, 32.2, 21.1, 20.7, 16.0, -0.5; IR (neat) 3400, 2960, 1650, 1400, 1240 cm^{-1}. Anal. Calcd. for $C_{15}H_{28}O_3Si$: C, 63.33, H, 9.92. Found : C, 63.44, H, 10.17. **38D**, (120 mg, 42%) ^{2}H-NMR ($CHCl_3$+ 2.5% $CDCl_3$, 46 MHz) δ 4.82 (0.5D), 1.03 (0.5D); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 104.2 (residual), 103.9 (t, *J*=25 Hz, CD), 20.7 (residual), 20.3 (t, *J*=18 Hz, CH_2D); IR (neat) 3420, 2940, 2870, 2130, 2080, 1450, 1240, 1040, 850 cm^{-1}. GC/CIMS *m/z* : 268 (MH^+-H_2O, 100).

3-(3-hydroxy-3-methylbutyl)-4-methyl-2-trimethylsilylmethylcyclopent-2-en-ol (39), (73 mg, 26%), solid m.p. : 93-95°C, ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.44 (m, 1H), 2.52 (m, 1H), 2.44 (dt, *J*=12.8, 7.2 Hz, 1H), 2.14 (td, *J*=13.2, 4.6 Hz, 1H), 2.04 (td, *J*=13.2, 4.6 Hz, 1H), 1.75 (m, 1 H), 1.65-1.55 (m, 3H), 1.32 (m, 1H), 1.26 (s, 6H), 1.15 (dt, *J*=12.8, 5.2 Hz, 1H), 1.04 (d, *J*=6.8 Hz, 3H), 0.02 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 139.9, 135.6, 79.2, 70.9, 42.0, 41.8, 38.5, 29.2, 29.1, 21.6, 20.7, 16.1, -0.5; IR 3400, 2940, 1680, 1200, 820 cm^{-1}. GC/CIMS *m/z* : 253 (MH^+-H_2O, 100). Anal. Calcd. for $C_{15}H_{30}O_2Si$: C, 66.61, H, 11.18. Found : C, 66.55, H, 11.14.

Radical cyclization of **40** :

See the general procedure above on a 1 mmol scale. Chromatography (PE:EtOAc, 90:10) afforded :

3-(3-*tert*-butyldimethylsilyloxypropyl)-4-methyl-2-trimethylsilylmethyl-2-cyclopenten-1-ol (41) (214 mg, 60%), ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.49 (m, 1H), 3.63 (t, *J*=5.9 Hz, 2H), 2.55 (m, 1H), 2.44 (dt, *J*=12.8, 7.1 Hz, 1H), 2.14 (m, 1H), 2.04 (m, 1H), 1.67-1.57 (m, 3H), 1.45 (m, 1H), 1.15 (dt, *J*=12.8, 5.1 Hz, 1H), 1.07 (d, *J*=6.6 Hz, 3H), 0.92 (s, 9 H), 0.07 (s, 6 H), 0.04 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 140.0, 135.5, 79.2, 63.3, 42.0, 38.5, 31.2, 26.0, 23.2, 20.7, 18.3, 16.0, -0.3, -5.2; IR 3340, 2940, 2850, 1650, 1450, 1250, 1095, 830 cm^{-1}. **41D**, (216 mg, 60%) ^{2}H-NMR ($CHCl_3$+ 2.5% $CDCl_3$, 46 MHz) δ 3.60 (0.42D), 1.60 (0.29D), 1.05 (0.29D); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 63.3 (residual), 63.1 (t, *J*=21 Hz, CHD), 31.2 (m), 20.7 (residual), 20.4 (t, *J*=19 Hz, CH_2D); IR (neat) 3350, 2950, 2850, 2140, 1650, 1460, 1250, 1100 cm^{-1}. CIMS *m/z* : 340 (MH^+-H_2O, 100).

Radical cyclization of **42** :

See the general procedure above on a 1 mmol scale. Chromatography (PE:EtOAc, 30:70) afforded :

3-(2-hydroxylethyl)-4-methyl-2-trimethylsilylmethyl-2-cyclopenten-1-ol (43), (155 mg, 68%), ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.49 (m, 1H), 3.70 (dt, *J*=10.2, 7.1 Hz, 1H), 3.63 (dt, *J*=10.2, 7.1 Hz, 1H), 2.50 (m, 2H), 2.36 (t, *J*=7.1 Hz, 2H), 1.60-1.70 (mAB, 2H), 1.19 (dt, *J*=12.8, 5.1 Hz, 1H), 1.10 (d, *J*=6.6 Hz, 3H), 0.05 (s, 9H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 138.8, 136.0, 78.9, 61.1, 42.0, 39.0, 30.4, 20.9, 16.2, -0.2; IR (neat) 3300, 2950, 1650, 1440, 1250, 1040, 850 cm^{-1}. Anal. Calcd. for $C_{12}H_{24}O_2Si$: C, 63.16, H, 10.53. Found : C, 63.27, H, 10.58. **43D**, (155 mg, 68%) ^{2}H-NMR ($CHCl_3$+ 2.5% $CDCl_3$, 46 MHz) δ 3.65 (0.15D), 1.05 (0.85D); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 20.9 (residual), 20.7 (t, *J*=19 Hz, CH_2D); IR (neat) 3300, 2940, 2160, 1650, 1405, 1240, 1030, 850 cm^{-1}. CIMS *m/z* : 212 (MH^+-H_2O, 100).

Radical cyclization of **44** :

See the general procedure above on a 1 mmol scale. Chromatography (PE:EtOAc, 85:15) afforded :

3-(2-*tert*-butyldimethylsilyloxyethyl)-4-methyl-2-trimethylsilylmethyl-2-cyclopenten-1-ol (45), (214 mg, 63%), ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.48 (m, 1H), 3.65 (td, *J*=9.2, 6.6 Hz, 1H), 3.55 (td, *J*=9.2, 6.6 Hz, 1H), 2.49 (m, 1H), 2.45 (dt, *J*=12.8, 7.6 Hz, 1H), 2.30 (m, 2H), 1.63-1.53 (mAB, 2H), 1.15 (dt, *J*=12.8, 5.2 Hz, 1H), 1.09 (d, *J*=6.4 Hz, 3H), 0.95 (s, 9 H), 0.10 (s, 6 H), 0.05 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 137.6, 137.1, 79.2, 62.0, 42.2, 39.2, 31.9, 26.1, 21.0, 18.5, 16.3, -0.5, -5.1; IR 3360, 2940, 2880, 1650, 1460, 1240, 1090, 860 cm^{-1}. **45D**, (205 mg, 60%) ^{2}H-NMR ($CHCl_3$+ 2.5% $CDCl_3$, 46 MHz) δ 3.60 (0.6D), 1.59 (0.2D), 1.10 (0.2D); IR (neat) 3300, 2940, 2840, 2150, 1460, 1240, 1080 cm^{-1}. CIMS *m/z* : 326 (MH^+-H_2O, 100).

Acknowledgement :

S. B. thanks Glaxo-Wellcome for a grant. Ms. Selma Sapmaz is acknowledged for running some of these experiments.

References and Notes

1. Magnol, E.; Malacria, M. *Tetrahedron Lett.* **1986**, 27, 2255-2256.
2. Malacria, M. *Chem. Rev.* **1996**, 96, 289-306.
3. Journet, M.; Malacria, M. *J. Org. Chem.* **1992**, *57*, 3085-3093.
4. Bogen, S.; Journet, M.; Malacria, M. *Synlett* **1994**, 958-960.
5. Bogen, S.; Malacria, M. *J. Am. Chem. Soc.* **1996**, *118*, 3992-3993.
6. Fensterbank, L.; Dhimane, A. L.; Wu, S.; Lacôte, E.; Bogen, M.; Malacria, M. *Tetrahedron* **1996**, *52*, 11405-11420.
7. a) Barton, D. H. R. *Pure and Appl. Chem.* **1968**, 1-15. b) Kalvoda, J.; Heusler, K. *Angew. Chem. Int., Ed. Engl.* **1964**, *3*, 501-526. c) Neale, R. S. *Synthesis* **1971**, 1-15.
8. Wolf, M. E. *Chem. Rev.* **1963**, *63*, 55-64.
9. For related remote functionalization of steroids using complexed halogen radicals, see : White, P.; Breslow, R. *J. Am. Chem. Soc.* **1990**, *112*, 6842-6847 and references therein.
10. For recent references, see : a) Robertson, J.; Peplow, M. A.; Pillai, J. *Tetrahedron Lett.* **1996**, *37*, 5825-5828. b) Borthwick, A. D.; Caddick, S.; Parsons, P. J. *Tetrahedron* **1992**, *48*, 10655-10666. c) Brown, C. D. S.; Simpkins, N. S.; Clinch, K. *Tetrahedron Lett.* **1993**, *34*, 131-132. d) Murphy, J. A.; Roone, J. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1349-1358. e) Sato, T.; Kugo, Y., Nakaumi, E.; Ishibashi, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1801-1809. f) Beckwith, A. L. J.; Storey, J. M. *J. Chem. Soc., Chem. Commun.* **1995**, 977-978. g) Bosch, E.; Bachi, M. O. *J. Org. Chem.* **1993**, *58*, 5581-5582.
11. 2-*O*-(2-bromoaryl)dimethylsilyl ethers: a) Curran, D. P.; Kim, D.; Liu, H. T.; Shen, W. *J. Am. Chem. Soc.* **1988**, *110*, 5900-5902. b) Schwartz, C. E.; Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 9272- 9284. c) Yamazaki, N.; Eichenberger, E.; Curran, D. P. *Tetrahedron Lett.* **1994**, *35*, 6623-26. Amides : d) Snieckus, V.; Cuevas, J.-C.; Sloan, C. P.; Liu, H. Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 896-898. e) Curran, D. P.; Yu, H.; Liu, H. *Tetrahedron* **1994**, *50*, 7343-7366. 2-bromo-4-methoxy phenyl ether : f) Curran, D. P.; Xu, J. *J. Am. Chem. Soc.* **1996**, *118*, 3142-3147.
12. Curran, D. P.; Shen W. *J. Am. Chem. Soc.* **1993**, *115*, 6051-6059.
13. Nedelec, J. Y.; Lefort, D. *Tetrahedron* **1975**, *31*, 411-417.
14. Masnyk, M. *Tetrahedron Lett.* **1997**, *38*, 879-882.
15. Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091-2115. Transannular examples: a) Winkler, J. D.; Hong, B-C. *Tetrahe dron Lett.* **1995**, *36*, 683-686. b) Boivin, J.; da Silva, E.; Ourisson, G.; Zard, S. Z. *Tetrahedron Lett.* **1990**, *31*, 2501-2504.
16. a) De Mesmaeker, A.; Waldner, P.; Hoffmann, P.; Hug, P.; Winkler, T. *Synlett* **1992**, 285-289. b) De Mesmaeker, A.; Waldner, A.; Hoffmann, P.; Winkler, T. *Synlett* **1994**, 330-332.
17. a) Brunckova, J.; Crich, D.; Yao, Q. *Tetrahedron Lett.* **1994**, *35*, 6619-6622. b) Crich, D.; Sun, S.; Brunckova, J. *J. Org. Chem.* **1996**, *61*, 605-615.
18. Huang, X. L.; Dannenberg, J. J. *J. Org. Chem.* **1991**, *56*, 5421-5424.
19. 1,3-H transfers : Damour, D.; Barreau, M.; Dhaleine, F.; Doerfingler, G.; Vuilhorgne, M.; Mignani, S. *Synlett* **1996**, 890-892. 1,4-H transfers : a) Wallace, T. J.; Gritter, R. J. *J. Org. Chem.* **1961**, *26*, 5256. b) Johnson, R. A.; Greene, F. D. *J. Org. Chem.* **1975**, *40*, 2186-2192. c) Lunazzi, L.; Placucci, G.; Grossi, L. *Tetrahedron* **1983**, *39*, 159-163. d) Lunazzi, L.; Placucci, G.; Grossi, L. *J. Chem. Soc., Perkin Trans. 2* **1981**, 703-707. e) Gilbert, B. C.; Parry, D. J.; Grossi, L. *J. Chem. Soc., Faraday Trans. 1* **1987**, 77-83. f) Brunton, G.; Griller, D.; Barclay, L. R. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 6803-6811. g) Lomas, J. S.; Briand, S. *J. Chem. Soc., Perkin Trans. 2* **1992**, 191-200. h) Montevecchi, P. C.; Navacchia, M. L. *Tetrahedron Lett.* **1996**, *37*, 6583-6586. i) Journet, M.; Malacria, M. *Tetrahedron Lett.* **1992**, *33*, 1893-1896. j) ref.11f. k) ref. 17.
20. Dorigo, A. E.; Houk, K. N. *J. Am. Chem. Soc.* **1987** 109, 2195-2197.
21. Delorme, D.; Girard, Y.; Rokach, J. *J. Org. Chem.* **1989**, *54*, 3635-3640.
22. a) Beckwith, A. L. J.; O'Shea, D. M. *Tetrahedron Lett.* **1986**, *27*, 4525-4528. b) Stork, G.; Mook, R., Jr. *Ibid.* **1986**, *27*, 4529-4532.
23. a) Pines, S. H.; Purick, R. M.; Reamer, R. A.; Gal, G. *J. Org. Chem.* **1978**, *43*, 1337-1342. b) Beckwith, A. L. J.; Boate, D. *J. Chem. Soc., Chem. Commun.* **1985**, 797-798. c) Curran, D. P.; Somayajula, K. S.; Yu, H. *Tetrahedron Lett.* **1992**, *33*, 2295-2298. d) Denenmark, D.; Winkler, T.; Waldner, A.; De Mesmaeker, A. *Tetrahedron Lett.* **1992**, *33*, 3613-3616. e) Curran, D. P.; Xu, J.; Lazzarini, E. *J. Chem. Soc., Perkin Trans. 1* **1995**, 3049-3059.
24. Beckwith, A. L. J.; Ingold, K. U. in *Free-Radical Rearrangements*, vol. 1, p. 226, 1980, de Mayo, P. Ed. Academic Press.
25. Huyser, E. S. *J. Org. Chem.* **1960**, *25*, 1820-1822.
26. For a relative radical stabilization scale, see: Merényi, R.; Janousek, H. G.; Viehe, H. G. in *Substituents Effects in Radical Chemistry*, 1986, p. 315, Ed. Viehe, H. G.; Janousek, H. G.; Merényi, R. D. Reidel Publishing Co., Louvain la Neuve.
27. Still, W. C.; Khan, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2423-2425.
28. Ma, D.; Lu, X. *Tetrahedron* **1990**, *46*, 6319-6320.
29. Lin, C. H.; Stein, S. J. *Synth. Commun.* **1976**, 503-508.
30. Asao, K.; Hideo, I.; Tokoroyama, T. *Tetrahedron Lett.* **1989**, *46*, 6401-6404.

(*Received in Belgium* 30 *May* 1997; *accepted* 30 *July* 1997)