

Synthesis of enynes and epoxyenynes by coupling: use of a new set of catalysts based on Pd–Ag salts

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Abstract

The new couple of catalysts Pd(PPh₃)₄ and AgI are very efficient for the coupling of vinyltriflates and terminal alkynes in the presence of a bulky amine in dimethylformamide at room temperature. Enynes and epoxyenynes are obtained in good to excellent yields. As illustrated with several examples, a wide variety of functional groups are well tolerated in the described conditions. Silver acetylides have been proposed as intermediate in this reaction. © 1998 Elsevier Science S.A. All rights reserved.

Keywords: Palladium; Silver; Epoxide; Vinyl triflate; Enynes; Coupling reactions

1. Introduction

A new class of antibiotic molecules has recently emerged, the enediynes, [1,2] which are among the most potent antitumor agents known to date. All of these molecules exhibit a common moiety, a conjugated enediyne system able, upon DNA complexation and chemical initiation, to rearrange with concomitant formation of a biradical species. Since it is complexed to the DNA minor groove, this biradical then abstracts hydrogen atoms from the deoxyribose part of DNA. Oxydation then leads to DNA cleavage, and eventually to cell death [1].

A few enediynes exhibit a further degree of complexity in their structure with the presence of an epoxide group adjacent to one of the triple bonds of the enediyne moiety included in a nine-membered ring. The neocarzinostatin **1** [3] and kedarcidin **2** [4] chro-

mophores and the recently discovered N1999A2 **3** [5] thus possess an epoxydienediyne system laid on a bicyclo[7.3.0]dodecane backbone (Scheme 1).

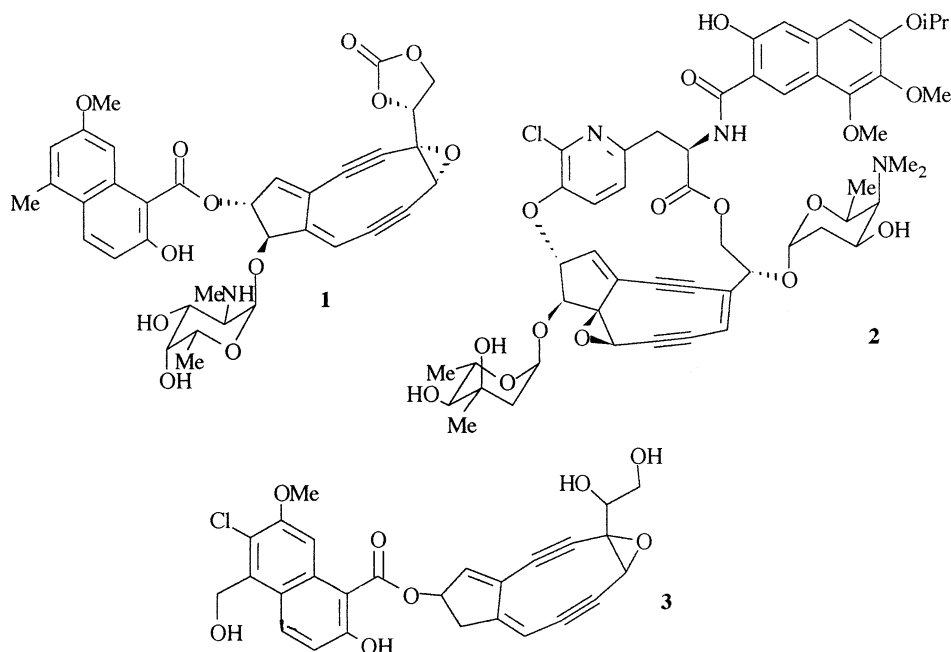
Since the epoxydienediyne system found in structures **1–3** is responsible for their particular mode of action and biological activity, we embarked upon a program devoted to the synthesis of this kind of system, with total synthesis and synthesis of analogs as the ultimate goals. As a preliminary part of this program, we intended to find a mild method to create the C–C bond between the multiple bonds of an epoxyenyn system (Scheme 2) since such coupling was unprecedented.

2. Synthesis of epoxyenynes and enynes by coupling

The synthesis of enynes by palladium-catalyzed coupling reaction between haloalkenes or enol triflates and alkynes is well described in the literature [6,7]. The Sonogashira–Linstrumelle procedure using both palladium complexes and copper salts as catalysts is amongst the most useful and has found many applications in the synthesis of natural products [1,6,8].

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Scheme 1.

Unfortunately, as we [9] and others [10] have experienced, this procedure proved to be inefficient for the direct synthesis of epoxyenynes starting from ethynyl oxiranes. In a preliminary work [9], we studied this reaction with two model compounds and introduced the use of silver iodide as a new mild cocatalyst. Indeed, in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium and a slight excess of diisopropylethylamine as base in dimethylformamide, silver iodide led to the clean formation of epoxyenynes in high yields. Other silver salts such as silver nitrate or carbonate proved to be efficient in this reaction, although lower yields were obtained [9].

In this communication, we described further investigations dealing with the scope and limitations of this new set of catalysts and we demonstrated here that these conditions allow for the synthesis of a wide variety of enynes and epoxyenynes. The probable *in situ* formation of silver acetylides as intermediates in this coupling reaction was also discussed.

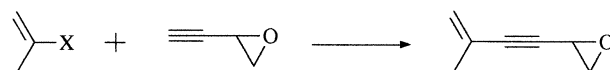
3. Synthesis of enynes

The usefulness of our method for enyne synthesis has been studied by coupling the vinyl triflate **4** derived from 4-*tert*-butylcyclohexanone, [11] with various alkynes. The choice of this triflate and of some alkynes was guided by the literature availability of similar or identical compounds used in more conventional coupling methods. Thus, direct comparison of the Pd–Ag catalytic system with others catalysts and/or other methods would be made possible.

Product structures were established by spectroscopic correlation with products previously prepared when possible or by full spectroscopic and analytic characterization (Section 7) in other cases. Nevertheless, the formation of the expected coupling products was evidenced in all cases by the presence in the crude ^1H -NMR spectra of a new vinyl signal characteristic of the conjugated enyne system.

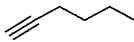
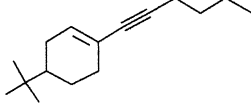
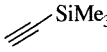
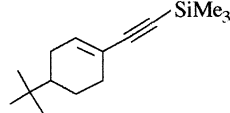
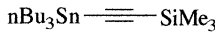
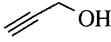
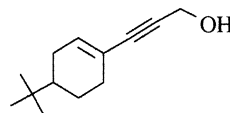
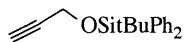
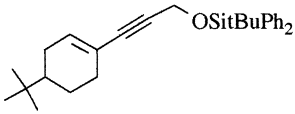
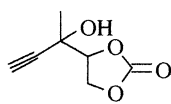
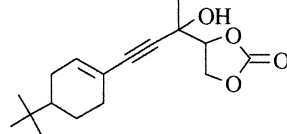
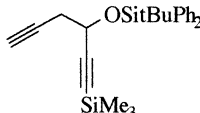
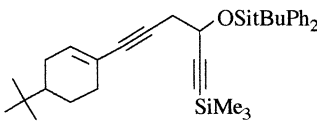
With 1-hexyne, the vinyl triflate **4** led to the corresponding enyne **5a** in high yield (entry 1, Table 1). It is noteworthy that this yield is by far better than the one reported by Stille et al. for the same coupling but with bis(triphenylphosphine)palladium dichloride as a catalyst and in the presence of triethylamine in DMF at 75°C (entry 2) [12]. Our conditions still gave a better yield of enyne than the best one reported [12] for the same starting compound and obtained by catalysis with tetrakis(triphenylphosphine)palladium in the presence or not of an excess of lithium chloride in THF at 60°C (75 or 50%, respectively, entry 3).

The coupling with trimethylsilylacetylene also gave the expected trimethylsilylenyne **5b** in a very efficient way with the Pd/Ag catalysts (entry 4). This product has already been obtained by coupling [13]. The reported procedure required the activation of the trimethylsilylacetylene as a stannyl acetylide in order to achieve an efficient coupling. Although the yields of



Scheme 2.

Table 1
Synthesis of enynes

$ \begin{array}{c} \text{Pd(PPh}_3)_4 \text{ 0.1 eq.} \\ \text{AgI 0.2 eq.} \\ \text{iPr}_2\text{NEt 1.25 eq.} \\ \text{DMF, r.t.} \end{array} $					
Entry	Alkyne	Reaction time	Product		Yield ^a
1		20 h		5a	82 %
2 ^b	"	24 h	"	5a	50 %
3 ^c	"	24 h	"	5a	75 %
4		20 h		5b	88 %
5 ^c		41 h	"	5b	90 %
6		2.5 h		5c	60 %
7		3.5 h		5d	83 %
8		20 h		5e	77 %
9		20 h		5f	80 %

^a Yields of isolated chromatographically pure products.

^b Reaction carried out [11] in the following conditions: PdCl₂(PPh₃)₂-NEt₃-DMF-75°C.

^c Reaction carried out [11,12] in the following conditions: Pd (PPh₃)₄-LiCl xs-THF-70°C

both coupling steps are quite similar (entry 5 vs. 4), our method allows for a direct coupling and thus avoids the additional activation step which lowers the overall yield of the reported method.

With propargyl alcohol, the formation of the enyne **5c** was very rapid compared to the precedings realized with purely hydrocarbonated compounds. However, slightly lower yields were obtained (entry 6 vs. 1, 4). Protection of the alcohol function simply solved this

minor drawback, significantly improving the yield while keeping a rapid, although slightly longer, reaction time (entry 7 vs. 6). The presence of an electronwithdrawing group at the propargylic position might well account for the increased reactivity of these two alkynes.

More fonctionalized alkynes have also been coupled. For example, a carbonate function, a group which is present in the neocarzinostatin structure (**1**, Scheme 1) was well tolerated. The carbonatoenyne **5e** was in-

deed obtained cleanly without noticeable change in yields (entry 8). However, the coupling rate was comparable to the one observed for the hydrocarbonated alkynes (entry 8 vs. 1, 4) despite the presence of an alcohol function at the propargylic position (entry 8 vs. 6, 7). A dissymmetrical 1,5-diyne [14] was also converted to the corresponding enediyne **5f** in high yield (entry 9) again with a rate comparable to the one observed for the hydrocarbonated alkynes (entry 9 vs. 1, 4).

4. Synthesis of epoxyenynes

In order to study the stability of the sensitive epoxide function toward this new procedure and to create the key epoxyenynone moiety present in the molecules **1–3**, we submitted various activated alkenes to the Pd–Ag coupling conditions in the presence of the epoxyalkynes **6a,b** [15] or **7** [16].

With the 4-*tert*-butylcyclohex-1-enyl triflate **4**, the expected epoxyenynone **10a** is obtained in high yield (entry 1, Table 2). As mentioned earlier, [9] use of the standard Sonogashira–Linstrumelle protocols led to extensive decomposition mainly of the epoxyacetylenic part of the molecules. In the Sonogashira or Linstrumelle condition, the presence of copper iodide proved to be deleterious and the expected product could only be isolated in low yield (entry 2). Since TLC monitoring indicated that the triflate **4** was almost unchanged while the epoxyalkyne **6a** was rapidly consumed, **6a** was slowly added over the other components of the reaction. With this modification, the yield was doubled but still modest and decomposition was still the major process (entry 3). Other Linstrumelle conditions ([7]d) without copper required longer reaction time and also led mainly to decomposition; nevertheless, the coupling product was detected and isolated in very low yield (entry 4). Clearly, our method using silver salts as cocatalyst greatly improves the direct coupling of epoxyalkyne with vinyl triflate.

Acetylenic epoxyalcohols can also be directly coupled without any protection as demonstrated by the reaction between 2,3-epoxypent-4-yn-1-ol **6b** [15] and the triflate **4** (entry 5). However, the yield of the epoxyenynol obtained was somewhat lower than the one obtained with the corresponding silylated product (entry 5 vs. 1), as observed in the case of the propargyl alcohol (Table 1, entry 7 vs. 6).

More functionalized vinyl triflates **8–9**, conjugated with a carbonyl group, [17] have also been coupled with the epoxyalkyne **6a**. The reactions led in an efficient way to the expected epoxyenynones **11a–12a** (entries 6, 7) as evidenced by their spectroscopic characteristics. (Section 7). These compounds proved to be very sensitive and although the NMR spectra of the crude mix-

tures showed in each case the sole presence of the expected product together with some starting materials left over, the purification by chromatography always led to some decomposition. Moreover, **12a** proved to be particularly prone to double bond isomerization. The stereochemistry of these enynones was deduced from the chemical shift of the vinyl proton which exhibits a typical [18] deshielding going from the *Z* to the *E* isomer (5.67 and 6.24 ppm, respectively).

Even 1,2-diethynyloxiranes can be directly linked to an alkenyl group through this new method. Indeed, when the monosilylated 1,2-diethynyloxirane **7**, obtained from **6a**, [16] was submitted to our standard conditions in the presence of the vinyl triflate **4**, the expected epoxyenediyne **13** was formed.

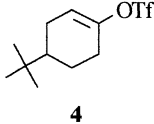
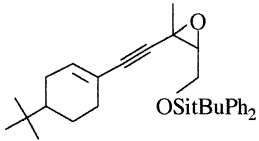
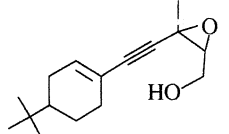
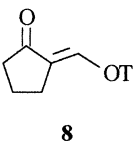
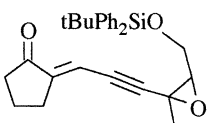
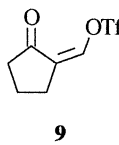
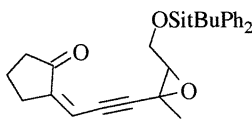
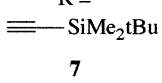
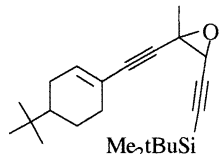
5. Mechanistic aspects

The coupling reaction leading to enynes is usually thought to proceed in three successive steps: oxidative addition, transmetallation and reductive elimination (oa, tm and re, respectively in Scheme 3). The key transmetallation step involves a reaction between an organopalladium (II) species generated through oxidative addition and a metal acetylide [6,19]. The acetylide can be directly incorporated in the reaction mixture as exemplified by the use of acetylenic tin reagents, [20] magnesium acetylides [21] and zinc acetylides [22] (Scheme 3, M = SnR₃, MgX, ZnX). In each of these cases, the acetylides must be independently prepared and stoichiometrically added to the coupling mixture.

Although widely used, the mechanistic bases of the Sonogashira–Linstrumelle coupling are less clear. It has been proposed ([7]a) that a copper acetylide would be generated in situ from the copper catalyst used and the terminal alkyne (Scheme 3, right part: M = Cu). However, to the best of our knowledge, no proof nor evidence have been obtained for such process. The copper acetylide so formed would then enter the palladium catalytic cycle at the transmetallation step, as the other metal acetylides mentioned above. The copper ion liberated during this step would be available for another reaction with another alkyne molecule yielding another copper acetylide. The overall process makes the copper also a catalyst.

When we observed that copper salts were responsible for degradation during coupling with epoxyalkynes, we looked for alternative catalysts. The analogy in electronic structure and chemical properties [23] led us to envisaged the use of silver salts instead of copper salts for coupling reactions. Since silver acetylides can be obtained from the corresponding terminal acetylenes using silver nitrate in the presence of ammonia, [23] we reasoned that amines could a priori be also effective in the formation of silver acetylides starting from terminal

Table 2
Synthesis of epoxyenynes

$ \begin{array}{c} \text{R} \\ \diagup \quad \diagdown \\ \text{C} \quad \text{C} \\ \diagdown \quad \diagup \\ \text{O} \end{array} + \begin{array}{c} \text{R}^1 \\ \diagup \quad \diagdown \\ \text{C} = \text{C} \\ \diagdown \quad \diagup \\ \text{R}^2 \quad \text{R}^3 \quad \text{X} \end{array} \xrightarrow[\text{DMF, r.t.}]{\text{Pd(PPh}_3)_4 \text{ 0.1 eq.}, \text{AgI 0.2 eq.}, \text{iPr}_2\text{NEt 1.25 eq.}} \begin{array}{c} \text{R}^1 \\ \diagup \quad \diagdown \\ \text{C} = \text{C} \\ \diagdown \quad \diagup \\ \text{R}^2 \quad \text{R}^3 \quad \text{C} \quad \text{C} \\ \diagdown \quad \diagup \\ \text{O} \end{array} $					
6a-b, 7		4, 8, 9	10a-b, 11-12a, 13		
Entry	Epoxide	Alkene	Reaction time	Product	Yield ^a
1	R = CH ₂ OSitBuPh ₂ 6a		20 h		10a 78 %
2 ^b	6a	4	30 mn	"	10a 24 %
3 ^c	6a	4	30 mn	"	10a 44 %
4 ^d	6a	4	2 d	"	10a 5 %
5	R = CH ₂ OH 6b	4	20 h		10b 55 %
6	6a		2 d		11a 40 %
7	6a		2 d		12a 52 %
8	R =  7	4	2 d		13 40 % ^e

^a Yields of isolated chromatographically pure products.

^b CuI used instead of AgI.

^c CuI used instead of AgI, and alkyne slowly added over the other compounds.

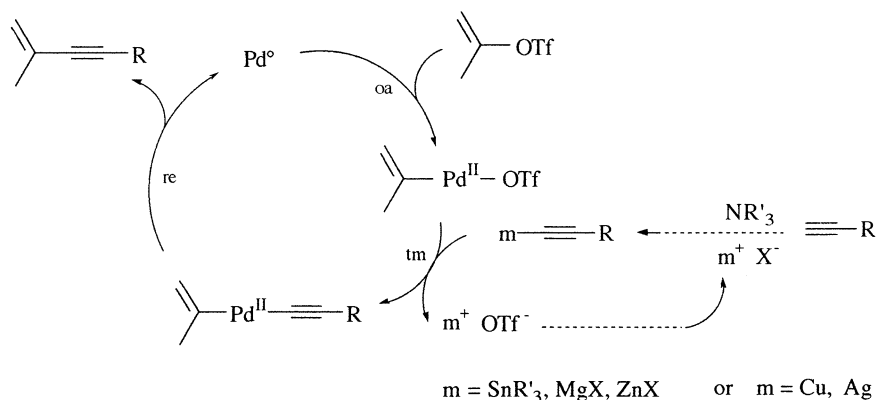
^d Piperidine used instead of AgI, DIPEA and DMF.

^e Quantitative if yield referred to triflate conversion.

acetylenes and silver salts. Furthermore, a few reactions were known to proceed under silver salts catalysis, the mechanisms of which probably involved silver-acetylene complexes [24] or even silver acetylides [25,26]. Therefore, a catalytic process comparable to the one involved in coupling reactions using copper salts could also be envisaged (Scheme 3, right part: M = Cu, Ag).

In our conditions, silver iodide may thus react with

alkyne and amine in DMF leading to a silver acetylide (Scheme 3, right part: M = Ag). [27] The latter would then behave as other metal acetylides and thus react in a transmetalation process with the organopalladium species resulting from oxidative addition of the vinyl triflate to a zerovalent palladium species. As silver acetylides are probable intermediates in the present coupling reaction, independent formation of silver



Scheme 3.

acetylides and their uses in coupling reactions are now actively pursued, and the results will be described in due course.

6. Conclusion

The Pd–Ag catalyzed reaction between enol triflates and alkynes provides a direct and efficient route to highly functionalized enynes. The examples described here highlight the versatility of this coupling procedure based on the new Pd–Ag set of catalysts. Good to excellent yields of enynes were obtained even with highly functionalized alkynes. Interestingly enough, acetylenic epoxydes can readily be coupled with various enol triflates providing highly functionalized epoxyenynes in a single step.

This procedure is a good alternative to the well-known Pd–Cu catalyzed coupling reaction and is far better for the direct synthesis of epoxyenynes. Works are currently in progress in our laboratory to explore further and understand better this reaction.

7. Experimental section

7.1. General

Yields are on isolated products. ^1H -NMR and ^{13}C -NMR spectra were recorded on a Bruker AC-250. IR spectra were recorded on a Spectrafile IRTM Plus MIDAC spectrometer. Mass spectra were measured on a Jeol D300 (70 eV) mass spectrometer. Melting points are uncorrected. Flash chromatography was carried out on silica gel purchased from Merck (0.040–0.063 mesh). Amines and DMF were dried and distilled from CaH_2 .

7.2. Typical procedure for coupling:

1-(4-*tert*-butyl-1-cyclohexenyl)-1-hexyne **5a**

A sample of diisopropylethylamine (154 μL , 0.89 mmol), tetrakis(triphenylphosphine) palladium (81 mg, 0.07 mmol) and silver iodide (33 mg, 0.14 mmol) were added at r.t. under argon to a solution of 4-*tert*-butyl-1-cyclohexenyl trifluoromethanesulfonate **4** (200 mg, 0.63 mmol) in dimethylformamide (10 ml). This solution was stirred for 10 min. in the dark, then 1-hexyne (100 μL , 0.85 mmol) was added. The reaction was monitored by TLC until the alkyne or the triflate was consumed. The mixture was then quenched with saturated aqueous ammonium chloride (10 ml) and extracted with ether (3×20 ml). The combined organic extracts were washed with water (3×10 ml), dried (MgSO_4) and concentrated. The crude product was purified by flash chromatography (silica gel-petroleum ether 100%) giving 125 mg (82%) of **5a** as a colorless liquid. Spectroscopic data of **5a** identical with the reported values [11].

7.3. Selected physical data of enynes **5c**, **5d**, **5e**, **5f**, **10a**, **10b**, **11a**, **12a**, **13**

3-(4-*Tert*-butyl-1-cyclohexenyl)-2-propyn-1-ol (**5c**): colorless oil. FT-IR (film): $\nu = 3353, 2218 \text{ cm}^{-1}$. ^1H -NMR (250 MHz, CDCl_3): $\delta = 0.85$ (9H, s), 1.09–1.30 (2H, m), 1.76–1.92 (2H, m), 2.05–2.21 (4H, m), 4.36 (2H, s), 6.07–6.13 (1H, m). ^{13}C -NMR. (62 MHz, CDCl_3): $\delta = 23.67, 27.02, 27.30, 30.55, 32.06, 43.13, 51.42, 84.81, 87.14, 119.86, 135.55$. H.R.M.S (E.I.) $m/e = 192.1507$ (192.1514 calc. for $\text{C}_{13}\text{H}_{20}\text{O}$).

3-(4-*Tert*-butyl-1-cyclohexenyl)-1-*tert*-butyldiphenylsilyloxy-2-propyne (**5d**): colorless oil. FT-IR (film): $\nu = 2220 \text{ cm}^{-1}$. ^1H -NMR (250 MHz- CDCl_3): $\delta = 0.85$ (9H, s), 1.07 (9H, s), 1.15–1.45 (2H, m), 1.78–1.95 (2H, m), 2.10–2.21 (3H, m), 4.44 (2H, s), 6.00–6.06 (1H, m),

7.33–7.45 (6H, m), 7.69–7.76 (4H, m). ^{13}C -NMR (62 MHz, CDCl_3): δ = 19.18, 23.75, 26.77, 27.13, 27.33, 30.54, 32.15, 43.22, 53.24, 85.13, 86.70, 120.22, 127.61, 129.65, 133.40, 134.97, 135.67. H.R.M.S (E.I.) m/e = 430.2708 (430.2692 calc. for $\text{C}_{29}\text{H}_{38}\text{OSi}$).

5-(4-*Tert*-butyl-1-cyclohexenyl)-3-methyl-4-pentyne-1,2,3-triol 1,2-carbonate (**5e**): colorless oil. FT-IR (film): ν = 3428, 2218, 1806–1777 cm^{-1} . ^1H -NMR (250 MHz, CDCl_3): δ = 0.85 (9H, s), 1.05–1.29 (2H, m), 1.56 (3H, s), 1.73–1.90 (2H, m), 2.02–2.20 (3H, m), 2.89 (1H, s), 4.47–4.65 (3H, m), 6.11–6.18 (1H, m). ^{13}C -NMR (62 MHz, CDCl_3): δ = 23.51, 26.39, 27.00, 27.32, 30.23, 32.06, 43.00, 66.45, 68.81, 80.02, 83.98, 87.91, 118.96, 137.22, 154.89. H.R.M.S (E.I.) m/e = 292.1674 (292.1674 calc. for $\text{C}_{17}\text{H}_{24}\text{O}_4$).

6-(4-*Tert*-butyl-1-cyclohexenyl)-3-*tert*-butyldiphenylsilyloxy-1-trimethylsilyl-1,5-hexadiyne (**5f**): colorless oil. FT-IR (film): ν = 2218, 2177 cm^{-1} . ^1H -NMR (250 MHz, CDCl_3): δ = 0.05 (9H, s), 0.85 (9H, s), 1.11–1.34 (2H, m), 1.75–1.92 (2H), 2.05–2.18 (3H, m), 2.73 (2H, br d, J = 6.5), 4.50 (1H, t, J = 6.5), 5.98–6.03 (1H, m), 7.32–7.46 (6H, m), 7.72–7.81 (4H, m). ^{13}C -NMR (62 MHz, CDCl_3): δ = –0.35, 19.37, 23.85, 26.91, 27.14, 27.31, 29.88, 30.84, 32.17, 43.31, 63.48, 83.38, 83.99, 89.71, 105.85, 120.67, 127.33, 127.51, 129.53, 129.63, 133.45, 133.63, 133.98, 135.99, 136.13.

Cis 5-(4-*tert*-butyl-1-cyclohexenyl)-1-*tert*-butyldiphenylsilyloxy-2,3-epoxy-3-methyl-4-pentyne (**10a**): colorless solid. M.p. 75°C. FT-IR (film): ν = 2222 cm^{-1} . ^1H -NMR (250 MHz, CDCl_3): δ = 0.85 (9H, s), 1.07 (9H, s), 1.00–1.26 (2H, m), 1.53 (3H, s), 1.73–1.85 (2H, m), 1.90–2.05 (3H, m), 3.13 (1H, t, J = 5.2), 3.87 (1H, dd, J = 11.5, J = 5.2), 3.93 (1H, dd, J = 11.5, J = 5.2), 5.91–5.97 (1H, m), 7.33–7.45 (6H, m), 7.68–7.72 (4H, m). ^{13}C -NMR (62 MHz, CDCl_3): δ = 19.22, 23.38, 23.60, 26.76, 27.06, 27.31, 30.30, 32.11, 43.10, 52.36, 63.91, 64.61, 83.62, 85.98, 119.47, 127.64, 129.61, 133.28, 133.59, 135.58, 136.26. H.R.M.S (E.I.) m/e = 486.2935 (486.2954 calc. for $\text{C}_{32}\text{H}_{42}\text{O}_2\text{Si}$).

Cis 5-(4-*tert*-butyl-1-cyclohexenyl)-2,3-epoxy-3-methyl-4-pentyn-1-ol (**10b**): colorless oil. FT-IR (film): ν = 2222 cm^{-1} . ^1H -NMR (250 MHz- CDCl_3): δ = 0.83 (9H, s), 1.05–1.30 (3H, m), 1.55 (3H, s), 1.75–1.90 (2H, m), 2.00–2.20 (3H, m), 3.12 (1H, dd, J = 6.1, J = 4.6), 3.81 (1H, dd, J = 12.2, J = 6.1), 3.89 (1H, dd, J = 12.2, J = 4.6), 6.10–6.15 (1H, m). ^{13}C -NMR (62 MHz, CDCl_3): δ = 23.50, 23.59, 27.03, 27.34, 30.40, 32.10, 43.07, 52.39, 62.57, 64.27, 83.39, 86.32, 119.35, 136.75. M.S (E.I.) m/e = 248 (M^+).

Cis (*E*)-2-(6-*tert*-butyldiphenylsilyloxy-4,5-epoxy-4-methyl-2-hexynylidene)-cyclopentanone (**11a**): yellow oil. FT-IR (film): ν = 2216 cm^{-1} . ^1H -NMR (250 MHz, CDCl_3): δ = 1.09 (9H, s), 1.59 (3H, s), 1.85 (2H, tt, J = 7.8, J = 7.4), 2.35 (2H, t, J = 7.8), 2.49 (2H, td, J = 7.4, J = 2.9), 3.23 (1H, t, J = 5.2), 3.90 (1H, dd, J = 11.4, J = 5.2), 3.93 (1H, dd, J = 11.4, J = 5.2), 6.24

(1H, t, J = 2.9), 7.32–7.41 (6H, m), 7.66–7.72 (4H, m). ^{13}C -NMR (62 MHz, CDCl_3): δ = 19.18, 19.18, 22.94, 26.71, 28.80, 38.31, 52.09, 63.81, 64.82, 81.77, 97.79, 110.94, 127.71, 129.74, 133.06, 133.36, 135.52, 148.70, 205.29.

Cis (*Z*)-2-(6-*tert*-butyldiphenylsilyloxy-4,5-epoxy-4-methyl-2-hexynylidene)-cyclopentanone (**12a**): yellow oil. FT-IR (film): ν = 2216 cm^{-1} . ^1H -NMR (250 MHz, CDCl_3): δ = 1.08 (9H, s), 1.62 (3H, s), 1.92 (2H, tt, J = 7.7, J = 7.2), 2.32 (2H, t, J = 7), 2.71 (2H, td, J = 7.2, J = 2.4), 3.20 (1H, dd, J = 5.4, J = 4.8), 3.97 (1H, dd, J = 11.7, J = 5), 4.07 (1H, dd, J = 11.7, J = 4.8), 5.67 (1H, t, J = 2.4), 7.34–7.43 (6H, m), 7.70–7.74 (4H, m). ^{13}C -NMR (62 MHz, CDCl_3): δ = 19.22, 19.79, 22.90, 26.77, 31.27, 39.05, 52.24, 63.92, 65.20, 81.77, 95.64, 110.43, 127.60, 129.53, 133.42, 133.67, 135.61, 147.44, 203.62.

Cis 6-(4-*tert*-butyl-1-cyclohexenyl)-1-*tert*-butyldimethylsilyl-3,4-epoxy-4-methyl-1,5-hexa-diyne (**13**): yellow oil. FT-IR (film): ν = 2222, 2174 cm^{-1} . ^1H -NMR (250 MHz, CDCl_3): δ = 0.13 (6H, s), 0.86 (9H, s), 0.95 (9H, s), 1.12–1.32 (2H, m), 1.55 (3H, s), 1.78–1.93 (2H, m), 2.09–2.26 (3H, m), 3.44 (1H, s), 6.15–6.21 (1H, m). ^{13}C -NMR (62 MHz, CDCl_3): δ = –4.74, 16.42, 22.81, 23.66, 25.99, 27.08, 27.41, 30.39, 32.14, 43.16, 53.36, 54.51, 81.42, 87.49, 88.07, 102.87, 119.54, 136.93. H.R.M.S (E.I.) m/e = 306.2537 (306.2535 calc. for $\text{C}_{23}\text{H}_{36}\text{OSi}$).

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