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Rapid and Easy Access to (*E*)-1,3-Enynes, 1,3-Diynes and Allenes Starting from Propargylic Acetals, Exploiting the Different Reactivity of Lithium and Mixed Lithium–Potassium Organometallic Reagents

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The treatment of propargylic acetals with various lithium and mixed lithium–potassium Schlosser reagents, has allowed a one-pot synthesis of (*E*)-1,3-enynes, 1,3-diynes and allenes, depending on the reaction conditions and the selected base. Various reaction conditions were investigated in order to control the selectivity of the reactions and to obtain pure products. The metallation–elimination sequence in the presence of a suitable electrophile has provided a linear route to functionalized (*E*)-conjugated enynes, diynes and allenes.

Introduction

Conjugated unsaturated systems such as 1,3-dienes, 1,3-enynes and diynes represent useful tools in organic synthesis and are used as valuable precursors to a variety of functionalized compounds as well as connective segments for the construction of carbon networks. Conjugated enynes and diynes have been used in the past as substrates in Pd^0-catalyzed [4π+2π] benzannulation,[1] Diels–Alder cycloaddition,[2] cross-metathesis[3] and thiocarbonylation to 2-thiocarbonyl-1,3-dienes.[4] Moreover, conjugated enyne and diyne systems are found in a number of natural products such as histrionicotoxin,[5] laurencin[6] and the neocarzinostatin chromophore.[7] Additionally, an increasing number of non-natural oligoynes and enynes have been prepared and investigated due to their peculiar optical, electrical and other material properties.[8] Several methods are available for the synthesis of enynes and diynes, many of which are based on the dimerization of 1-alkynes in the presence of transition-metal catalysts.[9] Unfortunately, the reaction scope is limited by the competitive formation of undesirable isomers. Conjugated enynes and diynes can also be prepared by Pd-catalyzed coupling of alkynyl or alkenyl halides and vinylmetal reagents.[10] Stereodefined enynes, enynols and dienynes have been synthesized with a Ti^{II} reagent starting from conjugated diynes.[11] Recent approaches to stereodefined conjugated enynes have involved the use of catalysis with Rh complexes.[12] Interestingly, 1,3-dienes and dienynes, as unique geometrical isomers, can be prepared by using zirconocene derivatives.[13] Among the syntheses that are not based on transition-metal catalysis, Karatholuvhu and Fuchs proposed an interesting use of vinylphosphonium halides in a basic medium.[14] Despite the large number of approaches found in the literature, there are notably only a few methods that permit the stereoselective construction of the enyne/diyne structure and, at the same time, the introduction of suitable substituents in a single step.[15] Owing to our interest and experience in the reactions of α,β-unsaturated acetals in the presence of mixed Schlosser superbases,[16] we decided to extend our studies to the employment of propargylic acetals as substrates. To the best of our knowledge, only three reports concerning base-promoted elimination reactions starting from propargylic acetals, otherwise known as the Viguier reaction,[17] have appeared in the literature.[18] We therefore decided to undertake a comprehensive study aimed at investigating the feasibility of propargylic acetals as potential substrates for the synthesis of functionalized conjugated unsaturated systems.

Results and Discussion

Recently we reported that the diethyl acetal of crotonaldehyde, when treated with the LIC-KOR superbase (equimolar mixture of BuLi and *t*BuOK), undergoes a conjugate elimination process affording the (*E*)-1-ethoxy-1,3-diene. The functionalization at the α-vinylic site was achieved in the presence of a further equivalent of base and a suitable electrophile. The overall process may account for the rapid

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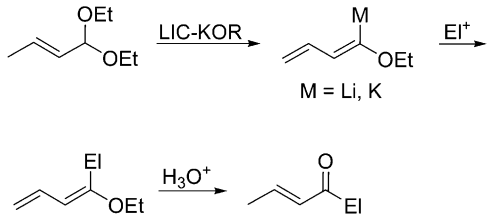
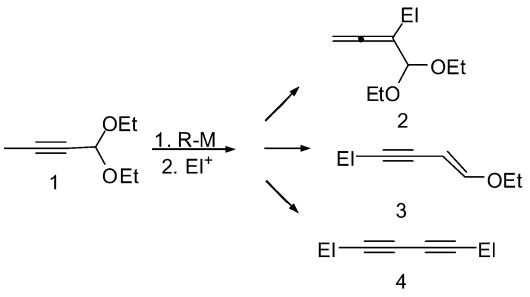
access to α,β-unsaturated carbonyl compounds by an umpolung approach (Scheme 1).[19]



Scheme 1. Synthesis of α-functionalized 1,3-dienes and α,β-unsaturated ketones, starting from crotonaldehyde diethyl acetal.

With these results in hand we decided to extend the study to the chemical behaviour of propargylic acetals in a basic medium and to investigate the feasibility of using these functional substrates for the one-pot synthesis of polyunsaturated systems. In order to optimize the reaction conditions, we chose to use the commercially available 1,1-diethoxybut-2-yne as a model acetal and pivalaldehyde as an electrophile in some preliminary screening experiments.

The structures of the products obtained are shown in Scheme 2 and the different reaction conditions applied are reported in Table 1.



Scheme 2. Base-promoted elimination processes and functionalization of 1,1-diethoxy-but-2-yne.

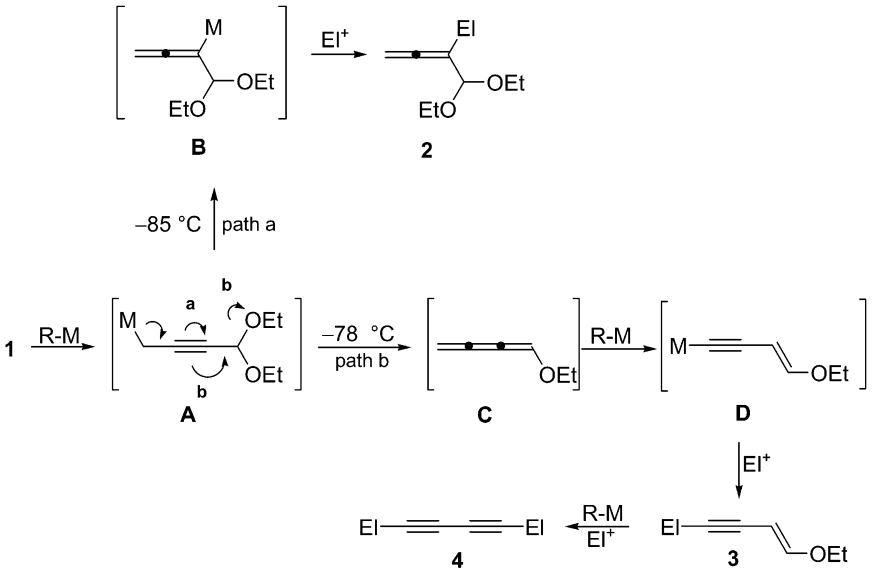
The first experiment was conducted by treating acetal **1** with 2.2 equiv. of the LIC–KOR reagent at –78 °C (Table 1, entry 1). After 2 h, 1 equiv. of pivalaldehyde was added and the temperature was raised to room temperature over 2 h. ^{1}H NMR analysis of the crude indicated the presence of enyne **3a** as a 2:1 mixture of *E*/*Z* isomers, as deduced from the value of the coupling constants (J = 12.9 and 6.3 Hz, respectively), and the diyne **4a**. The same procedure was applied in a further experiment in which the temperature was carefully controlled and kept at –85 °C after the addition of the electrophile (Table 1, entry 3). In this case the allenic acetal **2a** was isolated as the only product (75%); the structure was confirmed by the presence of a quaternary carbon at δ = 207.6 ppm in the ^{13}C NMR spectrum. The use of a smaller amount of base promoted the reaction as well, although acetal **2a** was recovered with a lower yield. The use of a large excess of LIC–KOR (Table 1, entries 5 and 6) induced a further elimination reaction and the formation of diyne **4a**. We then directed our efforts towards improving the puzzling results reported in entry 1. In order to refine the selectivity of the elimination process, we decided to switch to other bases: potassium hexamethyldisilazide (KHMDS) and BuLi (Table 1, entries 7 and 9) failed to promote the elimination and in both cases the starting acetal **1** was recovered unchanged. LIDA–KOR (LDA and *t*BuOK Table 1, entry 10) succeeded in metallating the propargylic position, but seemed to be even less selective than LIC–KOR and enyne **3** was recovered as a 1:1 mixture of *E*/*Z* isomers in low yield. However, LDA (entry 8) successfully allowed the stereoselective formation of substituted enyne **3** as the pure *E* isomer (72%).

In Scheme 3 a plausible mechanistic pathway accounting for the synthesis of the functionalized allenes, enynes and diynes is outlined. Initially, acetal **1** undergoes metal–hydrogen exchange at the propargylic site affording intermediate **A**. At –85 °C **A** rearranges to metallated allene **B** which, after the addition of a suitable electrophile, gives the functionalized allenic acetal **2** (path a). Alternatively, working at –78 °C, intermediate **A** undergoes conjugated elimination of EtO^- to afford cumulene **C** (path b). Addition of a further 1 equiv. of base promotes metallation and rearrangement to metallated (*E*)-4-ethoxybut-3-en-1-yn-1-ide **D**[20] which can be quenched with an electrophile to give functionalized enyne **3**. Finally, a larger excess of base and

Table 1. The different experimental conditions employed in the base-promoted elimination and functionalization of 1,1-diethoxybut-2-yne.

Entry	Base (equiv.)[a]	Conditions[b]	% Yield		
			2[c]	**3**[c]	**4**[c]
1	LIC–KOR (2.2)	2 h/–78 °C	–	45 (*E*/*Z*, 2:1)	25
2	LIC–KOR (1)	2 h/–78 °C	–	–	–
3	LIC–KOR (2.2)	2 h/–85 °C	75	–	–
4	LIC–KOR (1.5)	2 h/–85 °C	57	–	–
5	LIC–KOR (3.5)[d]	2 h/–78 °C	–	–	78
6	LIC–KOR (3.5)[d]	16 h/–78 °C to room temp.	–	–	78
7	KHMDS (2.2)	2 h/–78 °C	–	–	–
8	LDA (2.2)	2 h/–78 °C	–	72 (pure *E*)	–
9	BuLi (2.2)	2 h/–78 °C	–	–	–
10	LIDA–KOR (2.2)	2 h/–78 °C	–	25 (*E*/*Z*, 1:1)	–

[a] Relative to 1,1-diethoxybut-2-yne. [b] Reaction time and temperature after the addition of the electrophile. [c] Yield of isolated products. [d] 2 equiv. of pivalaldehyde were used.

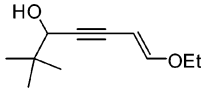
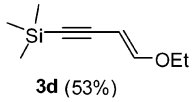
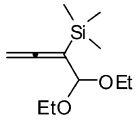
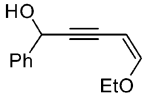
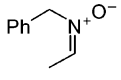
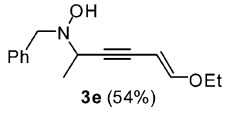
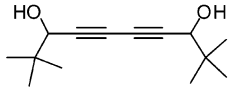
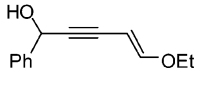
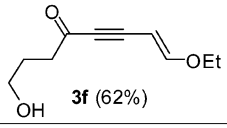
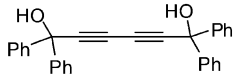
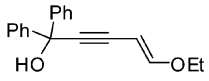
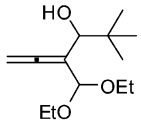
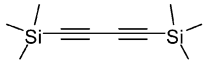
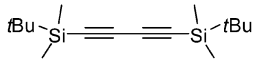


Scheme 3. Mechanistic pathways proposed for the base-promoted elimination reaction.

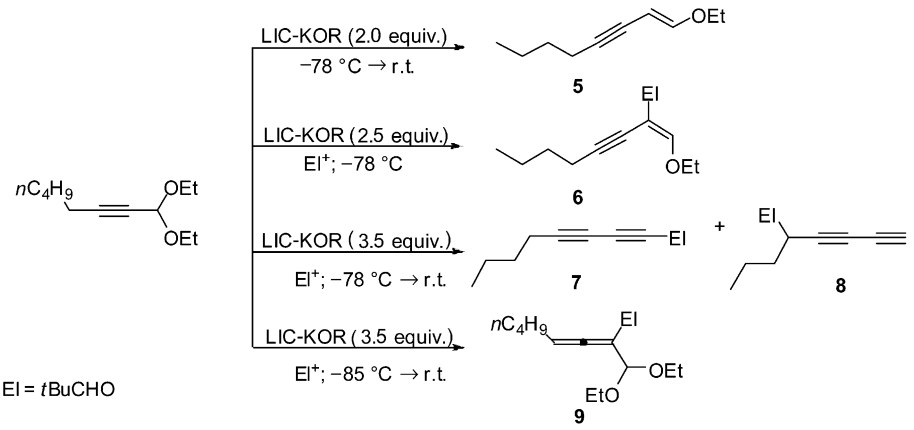
higher temperatures promote a further β-elimination of EtO^- and the formation of diyne **4**.

Summing up the results obtained so far, LDA selectively promotes the synthesis of the functionalized *E*-conjugated enynes **3a**–**f**, while an excess of superbase LIC–KOR induces a further metallation–elimination sequence that leads to the 1,4-difunctionalized 1,3-diynes **4a**–**d**. Finally, low temperatures, both in the presence of LDA and of LIC–KOR, hamper further elimination and functionalization steps so that allenes **2a** and **2b** can be isolated. It is noteworthy that in contrast to the results reported by Stracker and Zweifel,[15] in our experiments an excess of LDA (4 equiv.) does not promote the conversion of alkoxyenyne **3** into diyne **4**, even if the temperature is raised to room

Table 2. Products obtained by the reaction of 1,1-diethoxybut-2-yne with various electrophiles.[a]

El	Product	El	Product	El	Product
*t*BuCHO	 **3a** (85%)	TMSCl	 **3d** (53%)	TMSCl	 **2b** (56%)[b]
PhCHO	 **3b** (26 %)		 **3e** (54%)	*t*BuCHO	 **4a** (78%)
PhCHO	 **3b** (49 %)		 **3f** (62%)	Ph_2CO	 **4b** (68%)
Ph_2CO	 **3c** (56%)	*t*BuCHO	 **2a** (75%)	TMSCl	 **4c** (75%)
				*t*BuMe$_2$SiCl	 **4d** (77%)

[a] The reaction conditions applied are those described in Table 1 entry 8 for the enynes **3**, entry 6 for the diynes **4** and entry 3 for the allenes **2**. The yields reported are of the pure isolated material. [b] Yield refers to the crude reaction mixture, every attempt to isolate the product by column chromatography has been unsuccessful.



Scheme 4. Base-promoted elimination and functionalization of 1,1-diethoxyoct-2-yne.

temperature.[21] Once the experimental conditions that promote the selective formation of each of the possible products had been set up, we extended this approach to other classes of electrophiles (Table 2). Besides pivalaldehyde, benzaldehyde also exhibited a good reactivity. Notwithstanding this, it should be pointed out that this is the only example in which a functionalized enyne has been recovered as a mixture of *E*/*Z* isomers in a 2:1 ratio, as deduced by ^{1}H NMR analysis of the crude reaction mixture.

Good results were also obtained in the case of the encumbered ketone benzophenone; both enyne **3c** and diyne **4b** were obtained in good yields, 56 and 68%, respectively. Also the nitrone *N*-ethylidenebenzylamine *N*-oxide proved to be a good electrophile under the conditions of this work and the corresponding functionalized enyne was isolated. The formation of trialkylsilyl-functionalized enyne **3d** and diynes **4c** and **4d** is of remarkable synthetic value. As a matter of fact, **4c** and **4d** could be considered as a potential source of butadiyne, a useful, but unstable, intermediate.

The synthetic approach proposed has been extended to the α-acetylene acetal homologue 1,1-diethoxyoct-2-yne (Scheme 4). In the present case LDA failed to promote metallation at the propargylic methylenic site and the subsequent elimination reaction. Better results were obtained by using the LIC–KOR superbase. Also, in this case the choice of suitable experimental conditions allowed the selective formation of different functionalized unsaturated products. More precisely, 2.0 equiv. of superbase at –78 °C promoted the elimination–rearrangement sequence and enyne **5** was recovered as a mixture of the *E*/*Z* isomers in a 4:1 ratio. In the presence of an electrophile and of a slight excess of base 2-functionalized enyne **6** was recovered (68%) as the pure product.[22] A large excess of base prompted the substrate to undergo a further elimination and functionalization. Unfortunately metallation of the propargylic position competes with metallation of the terminal alkyne and a mixture of isomeric diynes **7** and **8** was recovered. As in the case of acetal **1**, precise control of the temperature allowed the allenic acetal **9** to be recovered.

In conclusion, we have reported herein a one-pot synthesis of functionalized (*E*)-enynes and symmetrical and unsymmetrical diynes. The syntheses start from readily available and economical propargylic acetals and it seems to be applicable to a wide range of electrophiles, thus providing a useful tool for the construction of regio- and stereo-defined enynes, diynes and their functionalized derivatives. Moreover, the products obtained are intriguing substrates for the further manipulation of the unsaturated conjugated systems.

Experimental Section

General: All solvents were degassed before use. Chromatographic separations were carried out under pressure on silica gel using flash-column techniques; R_f values refer to TLC carried out on 0.25 mm silica gel plates (Merck F254), visualization was accomplished by UV light (254 nm) or by spraying a solution of 5% (w/v) ammonium molybdate onto the plates and heating them to 200 °C or with 5% aqueous $KMnO_4$. All reactions involving air-sensitive reagents were performed under nitrogen in oven-dried glassware using a syringe/septum-cap technique. ^{1}H NMR spectra were recorded at 200 MHz and ^{13}C NMR spectra at 50.33 MHz. MS spectra were recorded at an ionizing voltage of 70 eV. THF was freshly distilled under argon from Na/benzophenone ketyl.

General Procedure for the Syntheses of Enynes (LDA): A solution of LDA, made from diisopropylamine (4 mmol, 564 μL) and BuLi (1.6 M in hexanes, 4 mmol, 2.5 mL) in THF (5 mL) at 0 °C for 15 min, was cooled to –78 °C and 1,1-diethoxybut-2-yne (2 mmol, 284 mg) in THF (2 mL) was added. The resulting mixture was stirred for 2 h during which time the temperature was raised to –40 °C. Afterwards, the reaction mixture was cooled again to –78 °C and a solution of the appropriate electrophile (2 mmol) was quickly added. The mixture was stirred for 2 h and the temperature allowed to rise to –10 °C. Then a saturated NH_4Cl solution (10 mL) was added, the mixture was extracted with Et_2O (3 × 10 mL), washed with water (10 mL) and brine (2 × 10 mL), and dried with anhydrous K_2CO_3. After filtration and evaporation of the solvent, the crude products were purified by flash column chromatography.

General Procedure for the Syntheses of Diynes (LIC–KOR): A solution of freshly sublimated *t*BuOK (7 mmol, 784 mg, 3.5 equiv.) in THF (7 mL) was cooled to –78 °C. 1,1-Diethoxybut-2-yne (2 mmol, 284 mg) in THF (2 mL) and BuLi (1.6 M in hexanes,

7 mmol, 4.37 mL) were added in quick succession and the mixture was stirred for 2 h during which time the temperature was raised to –40 °C. Afterwards the reaction was cooled back to –78 °C and the appropriate electrophile (4 mmol) in THF (2 mL) was added. The resulting mixture was stirred at –78 °C for 1 h, after which the temperature was allowed to rise to room temp. and the reaction was then stirred overnight. Then a saturated NH_4Cl solution (10 mL) was added, the mixture was extracted with Et_2O (3 × 10 mL), washed with water (10 mL) and brine (2 × 10 mL), and dried with anhydrous K_2CO_3. After filtration and evaporation of the solvent, the crude products were purified by flash column chromatography.

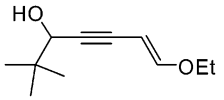
General Procedure for the Synthesis of Allenes 2a and 2b: Allenes **2a** and **2b** were synthesized both with LDA and LIC–KOR (see Supporting Information). The procedures were the same as described above except the temperature was strictly maintained at –85 °C.

General Procedure for the Synthesis of Enynes 5 (LIC–KOR): A solution of freshly sublimated *t*BuOK (4 mmol, 224 mg, 2.0 equiv.) in THF (4 mL) was cooled to –78 °C. 1,1-Diethoxyoct-2-yne (2 mmol, 396 mg) in THF (2 mL) and BuLi (1.6 M in hexanes, 4 mmol, 2.5 mL) were added in quick succession and the mixture was stirred for 2 h during which time the temperature was raised to room temp. The resulting mixture was stirred at that temperature for 1 h. Then a saturated NH_4Cl solution (10 mL) was added, the mixture was extracted with Et_2O (3 × 10 mL), washed with water (10 mL) and brine (2 × 10 mL), and dried with anhydrous K_2CO_3. After filtration and evaporation of the solvent, the crude products were purified by flash column chromatography.

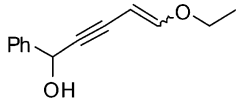
General Procedure for the Synthesis of Enyne 6 (LIC–KOR): A solution of freshly sublimated *t*BuOK (5 mmol, 560 mg, 2.5 equiv.) in THF (7 mL) was cooled to –78 °C. 1,1-Diethoxyoct-2-yne (2 mmol, 396 mg) in THF (2 mL) and BuLi (1.6 M in hexanes, 5 mmol, 3.2 mL) were added in quick succession and the mixture was stirred for 2 h during which time the temperature was raised to –40 °C. Afterwards the reaction was cooled back to –78 °C and pivalaldehyde (2 mmol) in THF (2 mL) was added. The resulting mixture was stirred at –78 °C for 1 h, a saturated NH_4Cl solution (10 mL) was added, the mixture was extracted with Et_2O (3 × 10 mL), washed with water (10 mL) and brine (2 × 10 mL), and dried with anhydrous K_2CO_3. After filtration and evaporation of the solvent, the crude products were purified by flash column chromatography.

General Procedure for the Synthesis of Diynes 7 and 8 (LIC–KOR): A solution of freshly sublimated *t*BuOK (7 mmol, 784 mg, 3.5 equiv.) in THF (7 mL) was cooled to –78 °C. 1,1-Diethoxyoct-2-yne (2 mmol, 396 mg) in THF (2 mL) and BuLi (1.6 M in hexanes, 7 mmol, 4.4 mL) were added in quick succession and the mixture was stirred for 2 h during which time the temperature was raised to –40 °C. Afterwards the reaction was cooled again down to –78 °C and the appropriate electrophile (4 mmol) in THF (2 mL) was added. The resulting mixture was stirred at –78 °C for 1 h, after which time the temperature was allowed to rise to room temp. and the reaction mixture was stirred overnight. Then a saturated NH_4Cl solution (10 mL) was added, the mixture was extracted with Et_2O (3 × 10 mL), washed with water (10 mL) and brine (2 × 10 mL), and dried with anhydrous K_2CO_3. After filtration and evaporation of the solvent, the crude products were purified by flash column chromatography.

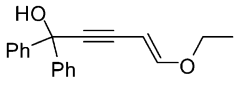
General Procedure for the Synthesis of Allene 9 (LIC–KOR): A solution of freshly sublimated *t*BuOK (7 mmol, 784 mg, 3.5 equiv.) in THF (7 mL) was cooled to –85 °C. 1,1-Diethoxyoct-2-yne (2 mmol, 396 mg) in THF (2 mL) and BuLi (1.6 M in hexanes, 7 mmol, 4.4 mL) were added in quick succession and the mixture was stirred for 1 h during which time the temperature was kept at –85 °C. Afterwards pivalaldehyde (2 mmol) in THF (2 mL) was added. The resulting mixture was stirred at –85 °C for 30 min. Then a saturated NH_4Cl solution (10 mL) was added, the mixture was extracted with Et_2O (3 × 10 mL), washed with water (10 mL) and brine (2 × 10 mL), and dried with anhydrous K_2CO_3. After filtration and evaporation of the solvent, the crude products were purified by flash column chromatography.



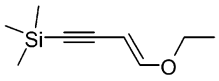
(*E*)-7-Ethoxy-2,2-dimethylhept-6-en-4-yn-3-ol (3a): Purified by flash chromatography (Et_2O/petroleum ether, 2:3, 1% Et_3N, R_f = 0.30) to give **3a** (310 mg, 85%) as a colourless oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 6.79 (d, J = 12.9 Hz, 1 H), 4.87 (d, J = 12.9 Hz, 1 H), 4.08 (s, 1 H), 3.78 (q, J = 7.0 Hz, 2 H), 1.90 (br. s, 1 H), 1.27 (t, J = 7.0 Hz, 3 H), 0.9 (s, 9 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 157.5 (d), 86.9 (s), 84.7 (d), 81.9 (s), 71.8 (d), 65.6 (t), 35.8 (s), 25.1 (q), 14.4 (q) ppm. MS: *m*/*z* (%) = 182 (34) $[M]^+$, 150 (46), 92 (100). $C_{11}H_{18}O_2$ (182.26): calcd. C 72.49, H 9.95; found C 72.39, H 9.83.



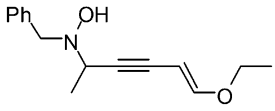
5-Ethoxy-1-phenylpent-4-en-2-yn-1-ol (3b): Purified by flash chromatography (Et_2O/petroleum ether, 1:4, 1% Et_3N) to give the *E* (198 mg, 49%) and *Z* (105 mg, 26%) isomers. *E* isomer: ^1H NMR (200 MHz, $CDCl_3$): δ = 7.54 (d, J = 6.7 Hz, 2 H), 7.42–7.25 (m, 3 H), 6.86 (d, J = 12.8 Hz, 1 H), 5.55 (s, 1 H), 4.93 (dd, J = 12.8, 1.1 Hz, 1 H), 3.79 (q, J = 7.0 Hz 2 H), 2.95–2.59 (br. s, 1 H), 1.29 (t, J = 7.0 Hz, 3 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 157.9 (d), 141.0 (s), 128.3 (d), 127.9 (d), 126.4 (d), 87.2 (s), 84.6 (d), 83.1 (s), 65.7 (t), 64.8 (d), 14.9 (q) ppm. MS: *m*/*z* (%) = 202 (39) $[M]^+$, 173 (53), 77 (100). $C_{13}H_{14}O_2$ (202.25): calcd. C 77.20, H 6.98; found C 77.46, H 6.65. *Z* isomer: ^1H NMR (200 MHz, $CDCl_3$): δ = 7.58 (d, J = 6.3 Hz, 2 H), 7.44–7.30 (m, 3 H), 6.36 (d, J = 6.4 Hz, 1 H), 5.61 (s, 1 H), 4.67–4.49 (d, J = 6.4 Hz, 1 H), 3.97 (q, J = 7.0 Hz, 2 H), 2.99 (br. s, 1 H), 1.35 (t, J = 7.01 Hz, 3 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 155.6 (d), 140.8 (s), 128.2 (d), 127.9 (d), 126.6 (d), 91.9 (s), 84.3 (d), 81.2 (s), 68.9 (d), 65.7 (t), 64.8 (d), 15.1 (q) ppm. MS: *m*/*z* (%) = 202 (48) $[M]^+$, 173 (50), 157 (52), 77(100).



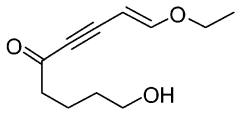
(*E*)-5-Ethoxy-1,1-diphenylpent-4-en-2-yn-1-ol (3c): Purified by flash chromatography (Et_2O/petroleum ether, 3:7, 1% Et_3N, R_f = 0.35) to give **3c** (312 mg, 56%). ^1H NMR (200 MHz, $CDCl_3$): δ = 7.52 (d, J = 7.6 Hz, 4 H), 7.29–7.12 (m, 6 H), 6.81 (d, J = 12.8 Hz, 1 H), 4.91 (d, J = 12.8 Hz, 1 H), 3.73 (q, J = 7.1 Hz, 2 H), 2.92 (br. s, 1 H), 1.21 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 158.6 (d), 145.7 (s), 128.7 (d), 127.7 (d), 126.3 (d), 90.09 (d), 84.7 (s), 83.9 (s), 74.8 (s), 65.7 (t), 14.1 (q) ppm. MS: *m*/*z* (%) = 278 (32) $[M]^+$, 233 (46), 204 (100). $C_{19}H_{18}O_2$ (278.35): calcd. C 81.99, H 6.52; found C 81.85, H 6.67.



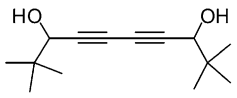
(*E*)-(4-Ethoxybut-3-en-1-ynyl)trimethylsilane (3d): Purified by flash chromatography (Et_2O/petroleum ether, 1:9, 1% Et_3N, R_f = 0.50) to give **3d** (179 mg, 53%). ^1H NMR (200 MHz, $CDCl_3$): δ = 6.85 (d, J = 12.8 Hz, 1 H), 4.88 (d, J = 12.8 Hz, 1 H), 3.77 (q, J = 7.0 Hz, 2 H), 1.27 (t, J = 7.0 Hz, 3 H), 0.20 (s, 9 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 158.5 (d), 101.8 (s), 92.1 (s), 85.3 (d), 65.6 (t), 14.3 (q), –0.1 (q) ppm. MS: m/z (%) = 168 (65) $[M]^+$, 153 (40), 103 (100). $C_9H_{16}OSi$ (168.31): calcd. C 64.23, H 9.58; found C 64.45, H 9.55.



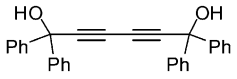
(*E*)-*N*-Benzyl-*N*-(6-ethoxyhex-5-en-3-yn-2-yl)hydroxylamine (3e): Purified by flash chromatography (Et_2O/petroleum ether, 1:1, 1% Et_3N, R_f = 0.30) to give **3e** (266 mg, 54%). ^1H NMR (200 MHz, $CDCl_3$): δ = 7.50–7.12 (m, 5 H), 6.91 (d, J = 12.9 Hz, 1 H), 5.23 (s, 1 H), 4.96 (dd, J = 12.9, 1.7 Hz, 1 H), 4.03 (d, J = 13.00 Hz, 1 H), 3.80 (m, 4 H), 1.41 (d, J = 6.9 Hz, 3 H), 1.31 (t, J = 7.0, 7.04 Hz, 3 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 157.5 (d), 143.2 (s), 137.1 (s), 129.4 (d), 128.1 (d), 127.2 (d), 84.8 (d), 82.2 (s), 65.6 (t), 61.5 (t), 54.3 (d), 19.4 (q), 14.4 (q) ppm. MS: m/z (%) = 245 (12) $[M]^+$, 230 (100), 214 (92), 90 (100). $C_{15}H_{19}O_2$ (231.31): calcd. C 81.99, H 6.52; found C 81.76, H 6.75.



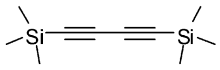
(*E*)-1-Ethoxy-9-hydroxynon-1-en-3-yn-5-one (3f): Purified by flash chromatography (Et_2O/petroleum ether, 1:1, 1% Et_3N, R_f = 0.30) to give **3f** (241 mg, 62%). ^1H NMR (200 MHz, $CDCl_3$): δ = 7.11 (d, J = 12.9 Hz, 1 H), 4.97 (d, J = 12.9 Hz, 1 H), 3.91 (q, J = 7.0 Hz, 2 H), 3.64 (t, J = 6.1 Hz, 2 H), 2.58 (t, J = 7.10 Hz, 2 H), 1.88–1.48 (m, 5 H), 1.33 (t, J = 7.0 Hz, 3 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 187.5 (s), 163.7 (d), 91.7 (s), 89.2 (d), 83.0 (s), 66.8 (t), 62.0 (t), 44.4 (t), 31.1 (t), 20.2 (t), 14.3 (q) ppm. MS: m/z (%) = 178 (100) $[M – 18]^+$, 95 (43), 77 (27). $C_{11}H_{16}O_3$ (196.25): calcd. C 67.32, H 8.22; found C 67.44, H 8.35.



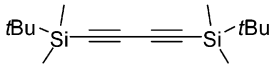
2,2,9,9-Tetramethyldeca-4,6-diyne-3,8-diol (4a): Purified by flash chromatography (Et_2O/petroleum ether, 3:7, 1% Et_3N, R_f = 0.30) to give **4a** (346 mg, 78%). ^1H NMR (200 MHz, $CDCl_3$): δ = 4.07 (d, J = 6.0 Hz, 1 H), 1.79 (d, J = 6.0 Hz, 1 H), 1.01 (s, 9 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 78.8 (s), 71.6 (d), 69.6 (s), 36.1 (s), 25.1 (q) ppm. MS: m/z (%) = 222 (5) $[M]^+$, 168 (65), 153 (40), 103 (100). $C_{14}H_{22}O_2$ (222.33): calcd. C 75.63, H 9.97; found C 75.34, H 9.85.



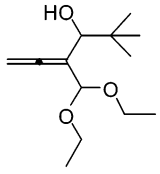
1,1,6,6-Tetraphenylhexa-2,4-diyne-1,6-diol (4b): Purified by flash chromatography (Et_2O/petroleum ether, 3:7, 1% Et_3N, R_f = 0.50) to give **4b** (563 mg, 68%). ^1H NMR (200 MHz, $CDCl_3$): δ = δ 7.68–7.48 (m, 8 H), 7.45–7.27 (m, 12 H), 3.17 (s, 2 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 143.6 (s), 128.2 (d), 127.9 (d), 125.9 (d), 82.5 (s), 74.8 (s), 71.0 (s) ppm. MS: m/z (%) = 414 (4) $[M]^+$, 396 (32), 309 (65), 231 (48), 105 (100). $C_{30}H_{22}O_2$ (414.50): calcd. C 86.93, H 5.85; found C 86.87, H 5.68.



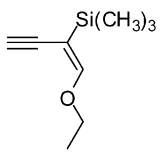
1,4-Bis(trimethylsilyl)buta-1,3-diyne (4c): Purified by flash chromatography (Et_2O/petroleum ether, 1:20, 1% Et_3N, R_f = 0.30) to give **4c** (291 mg, 75%). ^1H NMR (200 MHz, $CDCl_3$): δ = 0.15 (s, 18 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 85.8 (s), 85.7 (s), –0.1 (q) ppm. MS: m/z (%) = 194 (20) $[M]^+$, 179 (100), 73 (10). $C_{10}H_{18}Si_2$ (194.42): calcd. C 61.78, H 9.73; found C 61.87, H 9.68.



1,4-Bis(*tert*-butyldimethylsilyl)buta-1,3-diyne (4d): Purified by flash chromatography (Et_2O/petroleum ether, 1:20, 1% Et_3N, R_f = 0.30) to give **4d** (428 mg, 77%). ^1H NMR (200 MHz, $CDCl_3$): δ = 0.10 (s, 18 H), 025 (s, 12 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 86.6 (s), 86.6 (s), 25.8 (q), 16.5 (s), –5.1 (q) ppm. MS: m/z (%) = 278 (15) $[M]^+$, 221 (100), 179 (12), 73 (18). $C_{16}H_{30}Si_2$ (278.59): calcd. C 68.98, H 10.85; found C 68.83, H 10.78.

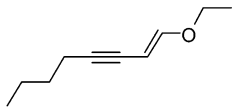


4-(Diethoxymethyl)-2,2-dimethylhexa-4,5-dien-3-ol (2a): Purified by flash chromatography (Et_2O/petroleum ether, 2:3, 1% Et_3N, R_f = 0.38) to give **2a** (341 mg, 75%). ^1H NMR (200 MHz, $CDCl_3$): δ = 4.95 (br. s, 2 H), 3.94 (d, J = 2.0 Hz, 1 H), 3.85–3.48 (m, 4 H), 1.25 (t, J = 6.89 Hz, 3 H), 0.95 (s, 9 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 207.6 (s), 102.9 (s), 102.4 (d), 79.9 (t), 77.5 (d), 63.6 (t), 62.6 (t), 36.1 (s), 27.1 (q), 15.9 (q) ppm. MS: m/z (%) = 211 (39) $[M – 17]^+$, 183 (80), 125 (60), 103 (100), 75 (45). $C_{13}H_{24}O_3$ (228.33): calcd. C 68.38, H 10.59; found C 68.66, H 10.45.

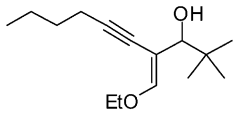


(*E*)-(1-Ethoxybut-1-en-3-yn-2-yl)trimethylsilane (3g): Purified by flash chromatography (Et_2O/petroleum ether, 1:15, 1% Et_3N, R_f = 0.88) to give (341 mg, 75%). ^1H NMR (200 MHz, $CDCl_3$): δ = 6.25 (s, 1 H), 3.94 (q, J = 6.5 Hz, 2 H), 3.2 (s, 1 H), 1.25 (t, J = 6.5 Hz, 3 H), 0.95 (s, 9 H) ppm. MS: m/z (%) = 168 (19) $[M]^+$, 123 (28), 73

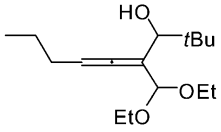
(100), 95 (70), 55 (15). $C_{13}H_{24}OSi$ (228.33): calcd. C 64.23, H 9.58; found C 64.43, H 9.65.



(*E*)-1-Ethoxyoct-1-en-3-yne (5): Purified by flash chromatography (Et_2O/petroleum ether, 1:4, 1% Et_3N, R_f = 0.58) to give **5** (204 mg, 67%). ^1H NMR (200 MHz, $CDCl_3$): δ = 6.73 (d, J = 12.81 Hz, 1 H), 4.89 (d, J = 12.81 Hz, 1 H), 3.76 (q, J = 7.03 Hz, 2 H), 2.26 (t, J = 2.20 Hz, 2 H), 1.52–1.41 (m, 4 H), 1.27 (t, J = 7.03 Hz, 3 H), 0.93–0.83 (t, J = 6.95 Hz, 3 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 156.2 (d), 88.1 (s), 85.7 (d), 75.8 (s), 65.3 (t), 30.9 (t), 21.8 (t), 18.9 (t), 14.4 (q), 13.4 (q) ppm. MS: *m*/*z* (%) = 152 (100) $[M]^+$, 109 (40), 95 (65), 75 (51), 57 (17). $C_{13}H_{24}O_3$ (228.33): calcd. C 68.38, H 10.59; found C 68.66, H 10.45.



(E)-4-(Ethoxymethylene)-2,2-dimethyldec-5-yn-3-ol (6): Purified by flash chromatography (Et_2O/petroleum ether, 1:4, 1% Et_3N, R_f = 0.48) to give **6** (168 mg, 75%). ^1H NMR (200 MHz, $CDCl_3$): δ = 6.36 (s, 1 H), 3.92 (q, J = 7.08 Hz, 2 H), 3.63–3.52 (d, J = 6.08 Hz, 1 H), 2.35 (t, J = 6.82 Hz, 2 H), 1.93 (d, J = 6.08 Hz, 1 H), 1.51–1.30 (m, 4 H), 1.25 (t, J = 6.82 Hz, 3 H) 0.96 (s, 9 H) superimposed on (t, J = 7.08 Hz, 3 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 152.3 (d), 101.25 (s), 97.85 (s), 79.33 (d), 74.28 (s), 68.68 (t), 36.00 (s), 30.61 (t), 26.50 (q), 21.80 (t), 19.37 (t), 14.99 (q), 14.25 (q) ppm. MS: *m*/*z* (%) = 238 (10) $[M]^+$, 223 (100), 195 (45), 181 (5), 69 (5). $C_{15}H_{26}O_2$ (228.33): calcd. C 75.58, H 10.99; found C 75.66, H 10.75.



4-(Diethoxymethyl)-2,2-dimethylnona-4,5-dien-3-ol (9): Purified by flash chromatography (Et_2O/petroleum ether, 1:4, 1% Et_3N, R_f = 0.48) to give **9** as a mixture of diastereoisomers (306 mg, 54%). ^1H NMR (200 MHz, $CDCl_3$): δ = 5.35 (t, J = 6.05 Hz, 1 H), 4.92 (s, 1 H), 3.92 (d, J = 4.04 Hz, 1 H), 3.73–3.45 (m, 4 H), 2.72 (d, J = 4.04 Hz, 1 H), 2.01 (m, 2 H), 1.85 (m, 4 H), 1.25 (t, J = 6.82 Hz, 6 H), 0.93 (s, 9 H) superimposed on (t, J = 7.08 Hz, 3 H) ppm. ^{13}C NMR (50.33 MHz, $CDCl_3$): δ = 202.2 (s), 137.55 (s), 103.13 (d), 102.96 (d), 94.60 (d), 60.52 (t), 35.98 (s), 32.36 (t), 29.64 (t), 25.06 (q), 23.09 (t), 15.92 (q), 14.75 (q) ppm. MS: *m*/*z* (%) = 284 (10) $[M]^+$, 223 (100), 195 (45), 181 (5), 69 (5). $C_{17}H_{32}O_3$ (284.44): calcd. C 71.79, H 11.34; found C 71.66, H 11.45.

Supporting Information (see also the footnote on the first page of this article): Experimental procedures and copies of the ^1H and ^{13}C NMR spectra of compounds **2a**, **3a**–**f**, **4a**–**d**, **5**, **6** and **9**.

Acknowledgments

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[20] Cumulene rearrangement to enyne in basic medium has already been reported, see: W. Pitsch, B. König, *Synth. Commun.* **2001**, *31*, 3135–3139.
[21] We suppose that, according to a suggestion of one of the referees, the $NH(iPr)_2$ newly formed in the reaction medium could trap the metallated enol ether intermediate so that no further conjugate elimination is possible. The additional equivalent of LDA therefore metallates the acetylenic position to give **D**.
[22] Starting from acetal **1** in the presence of 3 equiv. of LIC–KOR base and by using $(CH_3)_3SiCl$ as an electrophile, 1-ethoxybut-1-en-3-yn-2-yltrimethylsilane was captured when the reaction temperature was kept below –78 °C, even after the addition of the electrophile. In our opinion, these results corroborate the hypothesis that the base selectively metallates the β-vinyl site of the newly formed enyne. The formation of the conjugated system of diyne **4** can be therefore considered the driving force that leads to the observed selectivity. Notwithstanding this, we cannot exclude that **6** could be an intermediate which, in the presence of the base, undergoes a Fritch–Buttenberg–Wiechell rearrangement. We thank one of the referees for this suggestion.

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