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Preparation of silyl-protected γ -hydroxylated α,β -unsaturated acetylenic ketones and their reactions with some nucleophiles

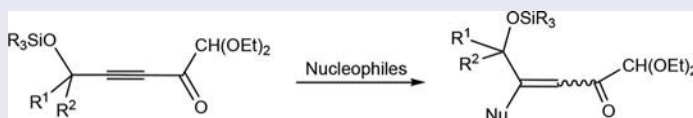
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ABSTRACT

A number of 5-siloxyated 1,1-diethoxy-3-alkyn-2-ones were prepared from the corresponding ketals. The *t*-butyldiphenylsiloxy derivatives were stable, whereas the trimethylsilyl analogs were unstable. The former compounds were reacted with diethylamine, lithium dimethylcuprate, and 1,3-propanedithiol and gave Michael adducts in good to very good yields. The amine and cuprate gave the conjugated alkenones, the former in a stereospecific manner (*Z*), the latter stereospecifically (*E*) in one case but otherwise stereoselectively with an *E* preponderance. With the dithiol bisaddition occurred, and the corresponding 1,3-dithiane was obtained in excellent yield. Attempts to make 1,3-dithianes from 1,3-propanedithiol and 1,1-diethoxy-4-diethylaminoalk-3-en-2-ones failed.

GRAPHICAL ABSTRACT



ARTICLE HISTORY

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KEYWORDS


Conjugate addition; conjugated acetylenic ketones; dimethylcopper lithium; 1,3-dithianes; propargylic alcohols; silyl protection

Introduction

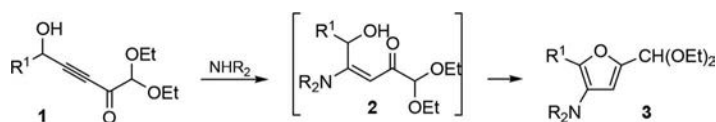
α,β -Unsaturated acetylenic ketones have proved to be valuable starting materials for the preparation of a wide range of organic compounds.^[1–5] A key reaction in many of these transformations is Michael addition, which primarily leads to formation of α,β -unsaturated alkenones,^[6] an important structural motif in its own right, but also excellent starting materials for the synthesis of more complex molecules. When a specific conjugated alkynone is reacted the final outcome depends on a number of factors, of which the presence of another reactive moiety in a favorable position relative to the ynone has appeared to be a useful feature. We have studied the reactions between a number of nucleophiles and a series of such alkynones, viz. 5-substituted 1,1-diethoxy-3-alkyn-2-ones, with this opportunity in mind, and we indeed observed that substituents at C-5 may facilitate multistep transformations leading to the formation of interesting stable secondary products.^[2–4]

An illustrative example of such a substituent is the hydroxyl group, which has appeared to enable **1** to form furans in good yields when treated with secondary amines.^[4] As

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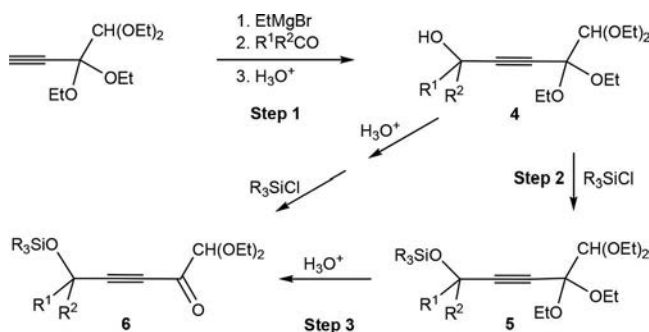
Scheme 1. Synthesis of 2-alkyl-3-dialkylamino-5-diethoxymethylfuran (3) by addition of dialkylamine to 1,1-diethoxy-5-hydroxy-3-alkyn-2-ones.

outlined in [Scheme 1](#), the reaction is believed to involve conjugated enone **2**, which is consumed quickly due to intramolecular hemiketalization, made possible by its *E* geometry and the resulting proximity of the OH and carbonyl groups, followed by dehydration. Thus, furan **3** is formed by default, not as a result of a reaction initiated by a controlled intervention with a specific outcome in mind. Consequently, if products other than furans are going to be formed, the OH group has to be protected so that no reaction occurs before the structural modifications required to facilitate the formation of other products have been carried out.

A large number of groups are available for protection of the hydroxyl group.^[7] Among the most versatile ones are the silyl ethers, which in general are easy to make and capable of surviving a range of reaction conditions prevailing during the application of many of the useful reagents.^[8] A single reaction performed some years ago indicated that this approach is promising,^[2] and we therefore wanted to convert a selection of 1,1,2,2-tetraethoxy-5-hydroxyalk-3-yne (**4**) into the corresponding silyl ether (**5**) and then 5-siloxyated 1,1-diethoxy-3-alkyn-2-ones (**6**) and investigate the reactivity of the α,β -unsaturated ketones. The results of this study are reported here.

Results and discussion

At the outset the plan was to convert **4** [obtained from 3,3,4,4-tetraethoxybutyne (TEB)^[9]] into silyl ethers **5** following the three-step synthesis summarized in [Scheme 2](#).^[2] Attempts were first made to synthesize some trimethylsilyl (TMS) ethers to estimate the robustness of the silylation (step 2) and the stability of the siloxy group during the deketalization (step 3). The outcome of step 2 appeared to be very sensitive to the method applied and the yields were often poor; thus, when 1,1,2,2-tetraethoxyundec-3-yn-5-ol (**4d**) and 6,6,7,7-tetraethoxy-5-ethylhept-4-yn-3-ol (**4g**) were reacted, yields in the 6–84% range



Scheme 2. Synthesis of 5-siloxyated 1,1-diethoxyalk-3-yn-2-ones (**6**) from TEB.

were obtained. The best results were achieved when a small amount of dimethylsulfoxide (DMSO) was added, a measure recommended by Visser et al.,^[11] and under these conditions the tetramethylsilane (TMS)–ether derivatives of **4d** and **4g** were easily available in around 80% yield. Next, deketalization was carried out following several literature procedures,^[2,12] but unfortunately, without exception, the desired reaction was accompanied by simultaneous desilylation so that the corresponding alcohols were completely regenerated in both cases. A solution to this problem was envisaged to be to switch steps 2 and 3, and when this strategy was implemented using **4g**, the corresponding protected ketone, 1,1-diethoxy-5-ethyl-5-trimethylsiloxyhept-3-yn-2-one (**6g**), was indeed obtained in 78% overall yield.

On the basis of these results it was decided to apply *t*-butyldiphenylsilyl (TBDPS) ethers instead since such ethers are about 100 times more stable to hydrolysis than *t*-butyldimethylsilyl ethers, which in turn are about 10⁴ times more stable than the TMS analogs.^[13] That change turned out to be a success; not only were the propargylic alcohols converted to the corresponding TBDPS ethers in better than 80% yield in all cases but one, but also the deketalization proceeded smoothly and furnished 5-siloxyated conjugated alkynones **6**, in almost quantitative yield in the best cases (Table 1).

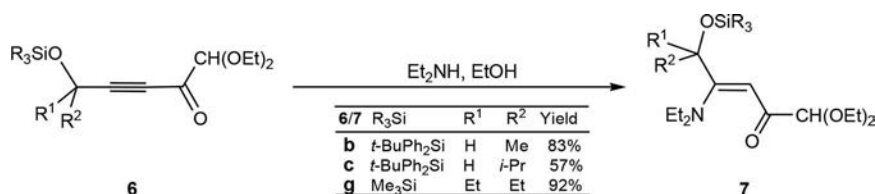
With silyl-ether-protected 1,1-diethoxy-5-hydroxy-3-alkyn-2-ones at hand Michael additions were performed with diethylamine, lithium dimethylcuprate (the Gilman cuprate), and 1,3-propanedithiol, all of which have been shown to react smoothly with similar alkynes.

The highest selectivity was achieved with the amine, which appeared to undergo monoaddition and afford the corresponding 4-diethylamino-3-alken-2-ones (**7**) in a stereospecific manner in excellent yields whether reacted with 5-trimethylsiloxy- or 5-(*t*-butyldiphenyl)siloxy-substituted 1,1-diethoxyalk-3-yn-2-ones (**6**) (Scheme 3). Comparison of the ¹H NMR data for **7** (chemical shifts and allylic coupling constants between the protons attached to C-3 and C-5) with available literature data^[14] gave no basis to draw a conclusion regarding the stereochemistry of these Michael adducts, but by performing nuclear Overhauser spectroscopy (NOESY) experiments it was unequivocally proved that **7** exhibited *Z* configuration in all cases. On one hand, this conclusion is founded on the presence of mutual enhancement of the signals due to the olefinic proton, hydrogen atoms in the alkyl group(s) attached to C-5, and all the hydrogens in the diethoxymethyl moiety; on the other hand, it is founded on the complete absence of any nuclear Overhauser enhancement of the signals due to the diethylamino group attached to C-4.

Me₂CuLi^[15] also underwent monoaddition to **6** and gave the corresponding 1,1-diethoxy-4-methyl-3-alken-2-ones (**8**) in up to excellent yield (Table 2). The reaction

Table 1. Isolated yields of siloxylated acetylenic ketals **5** and ketones **6** with R₃Si = *t*-BuPh₂.

R ¹ , R ²	Step 2 product/ isolated yield (%)	Step 3 product/ isolated yield (%)
H,H	5a /94	6a /56
Me,H	5b /82	6b /80
<i>i</i> -Pr,H	5c /82	6c /97
<i>n</i> -Hex,H	5d /81	6d /94
Me,Me	5e /82	6e /92
CH ₂ (CH ₂) ₃ CH ₂	5f /53	6f /70



Scheme 3. Addition of diethylamine to silyl ether-protected 1,1-diethoxy-5-hydroxy-3-alkyn-2-ones (6).

was stereospecific in one case only, when 5-(*t*-butyl)diphenylsiloxy-1,1-diethoxypent-3-yn-2-one (**6a**) was reacted; otherwise the transformation was stereoselective with a preponderance, up to six times at the most (for **6f**), for the isomer with the lower R_f value (Table 2). This lack of specificity is not surprising because the accepted intermediates, copper enolates, have been shown to equilibrate at a rate that is sensitive to solvent, temperature, concentration, complexation, and reaction time.^[16] As a result α,β -unsaturated olefinic carbonyl compounds with *E/Z* ratios approaching 1:1 have been obtained even in cases when the cuprate addition to the C-C triple bond is believed to be stereospecific.^[17]

Two of the three substituents attached to the C-C double bond in **8** are quite polar, and the overall polarity of the *E* isomer and the *Z* isomer of **8b–8f** should therefore be so different that separation of the isomers should be feasible. Screening of a number of solvents and solvent mixtures showed that such separation was indeed possible, but some eluents resulted in such a significant loss of material when flash chromatography (FC) was performed that they were unsuitable. Dichloromethane appeared to be the best choice in our case, and when this eluent was used, the isomers were easily separated, even on a gram scale, without loss of significant amounts.

For two of the alkenes, **8b** and **8f**, the stereochemistry could be settled based on the coupling constant for the CH₃-C=C-H structural motif. In such a spin system the allylic coupling (⁴*J*) is expected to have a larger absolute value when the olefinic hydrogen atom and the methyl group have a *cis* relationship than a *trans*, i.e., $|^4J_{cis}| > |^4J_{trans}|$.^[14,18] Since the coupling is larger for the minor isomer for both **8b** and **8f**, viz., 1.2 Hz compared to 0.9 Hz

Table 2. Synthesis of *E* and *Z* isomers of 1,1-diethoxy-4-methyl-3-alken-2-ones (**8**) by treating **6** with Me₂CuLi.

6 (R ¹ , R ²)	8, smaller R_f	8, larger R_f	ΔR_f	<i>E/Z</i>
	Product/isolated yield (R_f)	Product/isolated yield (R_f)		
6a (H, H)	<i>E</i> - 8a /39% (0.22)	— ^a	—	100:0
6b (Me, H)	<i>E</i> - 8b /49% (0.16)	<i>Z</i> - 8b /34% (0.34)	0.18	59:41
6c (<i>i</i> -Pr, H)	<i>E</i> - 8c /55% (0.24)	<i>Z</i> - 8c /41% (0.45)	0.21	57:43
6d (<i>n</i> -Hex, H)	<i>E</i> - 8d /48% (0.35)	<i>Z</i> - 8d /45% (0.62)	0.27	52:48
6e (Me, Me)	<i>E</i> - 8e /73% (0.23)	<i>Z</i> - 8e /27% (0.44)	0.21	73:27
6f ((CH ₂) ₅)	<i>E</i> - 8f /63% (0.27)	<i>Z</i> - 8f /11% (0.45)	0.18	85:15

^aThis isomer was not detected.

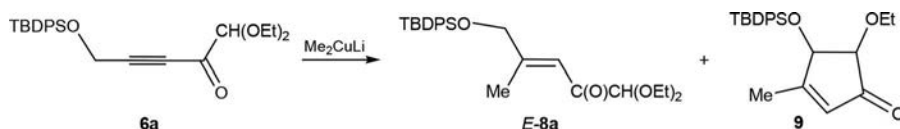
for **8b** and 1.1 Hz compared to < 0.5 Hz for **8f**, it was concluded that the *E* isomer predominates for both these olefins.

For the other alkenes the signals due to the allylic moiety appeared as broad singlets, conceivably caused by van der Waal interactions between the $\text{CH}_3\text{-C=C-H}$ structural motif and the two sterically demanding substituents attached to the olefinic carbon atoms, so no coupling constants could be extracted from the spectra. However, due to the fact that the polarity of the *Z* isomers ought to be similar for **8a–8f** and larger than the polarity of the corresponding *E* isomers of **8a–8f**, it is reasonable to assume that the relative retention for the *E* and *Z* isomers of each compound should be roughly the same under identical chromatographic conditions. That is the case for **8b** and **8f**, which, respectively, show R_f values 0.34 and 0.45 for the *Z* isomers and 0.16 and 0.27 for the corresponding *E* isomers. As argued above, **8c–8e** are expected to show the same relationship, and on the basis of the data in Table 2 it is concluded that these compounds as well are formed with *E* isomer predominance.

As mentioned, the reaction between **6a** and Me_2CuLi appears to be a special case. When this compound was reacted, thin-layer chromatographic (TLC; CH_2Cl_2) analysis of the residue after workup showed one spot, which suggested that one product had been formed. However, when the ^1H NMR spectrum of the product mixture was recorded it became clear that at least two major products were obtained. Attempts to separate the products were only partially successful; whereas the main product was obtained essentially pure in 39% yield the second product had to undergo several purifications, with significant loss of material, before a reasonably pure sample became available. When the ^1H NMR spectrum of the purified sample of the main product was compared with the spectra of the *E* and *Z* isomers of **8b–8f**, the chemical shifts of the most NMR-sensitive protons in the main product (the protons at C-3 and C-5) are much closer to those exhibited by the *E* isomers of the analogs than to those of the *Z* isomers. This indicates that **6a** furnishes only *E*-**8a**, and this conclusion is supported by the fact that the methyl group and the olefinic proton both give rise to a narrow singlet, which precludes the presence of allylic coupling. Finally, it is noteworthy that the R_f value for the compound under standard conditions (SiO_2 , CH_2Cl_2) is close to the values exhibited by the *E* isomers of **8b–8f** but much smaller than the values for the *Z* isomers (Table 2).

The other major product from **6a** gave MS, IR, and NMR spectra, which deviated in an indicative way from those obtained for the *E* and *Z* isomers of **8**. First, its molecular formula is reduced with $\text{C}_2\text{H}_6\text{O}$, which, according to the NMR spectra, is due to loss of ethanol. Second, prominent absorptions in the IR spectrum (1714 cm^{-1}) and the ^{13}C spectrum (203 ppm) are well off the values found in the spectra for *E/Z*-**8**, viz. $1688\text{--}1699\text{ cm}^{-1}$ and $193\text{--}196\text{ ppm}$, respectively. These differences are very informative; not only do they clearly indicate that the other product is cyclic, they also suggest that the product is a 2-cyclopentenone derivative.^[19,20] On the basis of this insight, the interpretation of the ^1H NMR, ^{13}C NMR, COSY, and heteronuclear single quantum coherence (HSQC) spectra becomes rather straightforward and leads to the unequivocal conclusion that the other main product is 4-(*t*-butyl)diphenylsiloxy-5-ethoxy-3-methylcyclopent-2-enone (**9**) (Scheme 4).

The reason for the exceptional behavior of **6a** in the reaction with Me_2CuLi is not clear, but it might be due to conformational effects caused by the presence of a methylene group at C-5 instead of the alkylated methylene group present in this position in **6b–6f**. When C-5 is not alkylated, a methylene proton in this position becomes much more available for abstraction, and this opens up for the reaction sequence summarized in Scheme 5. The first step is *cis* attack of lithium dimethylcuprate on the triple bond, which presumably gives

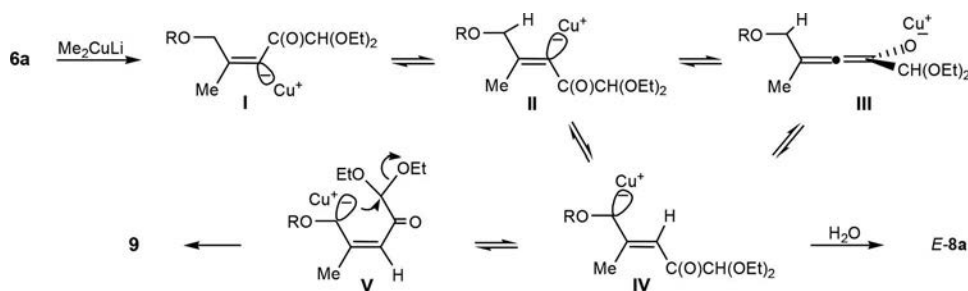


Scheme 4. Treatment of **6a** with lithium dimethylcuprate; TBDPS = (*t*-butyl)diphenylsilyl.

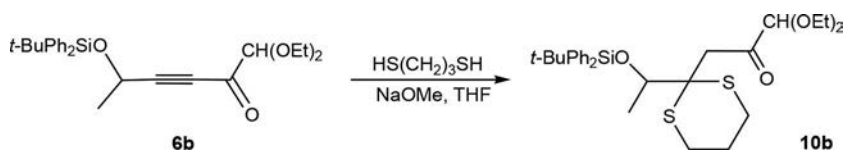
C-copper enolate **I**.^[16,17] This intermediate equilibrates with its *trans* isomer (**II**), which is capable of abstracting a propargylic proton directly or via its O-copper enolate (**III**), and forms carbanion **IV**. This carbanion will give *E*-**8a** upon hydrolysis, but it can also isomerize, because of its allylic nature, to its geometrical isomer **V**, which can undergo cyclization by intramolecular carbanion attack of the acetal moiety in an $\text{S}_{\text{N}}2$ type reaction with ethoxide as the leaving group and furnish **9** as a by-product. Since similar substitutions usually require borontrifluoride activation,^[21] the nucleophilicity of the carbanion in **V** is enhanced by the α -alkoxy group whereas the electrophilicity of C-1 is increased by the neighboring conjugated keto moiety.

The last nucleophile to be applied was 1,3-propanedithiol, which has been proved to undergo bis-addition with a range of α,β -unsaturated acetylenic ketones and give the corresponding 1,3-dithiane in very good yields.^[5] Again 5-(*t*-butyl)diphenylsiloxy-1,1-diethoxyhex-3-yn-2-one (**6b**) was used as a test case and as previously observed, the primary product was unstable due to an intramolecular reaction which furnished 3-(2-(1-(*t*-butyl)diphenylsiloxyethyl)-1,3-dithian-2-yl)-1,1-diethoxypropan-2-one (**10b**) in 82% yield (Scheme 6). This and similar 1,3-dithianes will now be used to prepare modified carbohydrates following the strategy applied for some time in our research group.

A final comment regarding the ability of 1,3-propanedithiol to undergo conjugate addition with conjugated ketones is warranted. From the literature,^[22] it is known that this dithiol can react with β -amino-substituted α,β -unsaturated ketones in a process encompassing three consecutive steps, viz. intermolecular sulfide addition, amine elimination, and intramolecular sulfide addition, which gives the corresponding 1,3-dithianyl ketone. If this is a general, robust reaction it is reasonable to believe that 5-(*t*-butyldiphenyl)siloxy-4-diethylamino-1,1-diethoxyhex-3-en-2-one (**7b**) would react smoothly and give **10b**, but this was not achieved even under conditions recommended for Michael additions to conjugated alkenyl and alkynyl ketones.^[5] Obviously, the reactivity is critically influenced by the properties of the amino group, an observation that merits further study.



Scheme 5. A sequence of equilibrations and transformations explaining the formation of *E*-**8a** and **9** upon treatment of **6a** with Me_2CuLi ; TBDPS = (*t*-butyl)diphenylsilyl.



Scheme 6. Bisaddition of 1,3-propanedithiol to conjugated ketone **6b**.

Experimental

Infrared (IR) spectra were run on a Nicolet Impact 410 IR spectrophotometer or Nicolet 380 FT-IR spectrophotometer. NMR spectra were recorded on Bruker Spectrospin spectrometers (DPX 400 MHz and DPX 500 MHz). Chemical shifts are reported in parts per million (ppm) downfield from internal tetramethylsilane (TMS). Thin-layer chromatographic (TLC) analyses of the reaction mixtures were performed with silica gel (60 F254) on aluminum sheets with mixtures of hexanes (a commercial mixture of isomeric hexanes) and ethyl acetate as the mobile phase. Flash chromatography (FC) was carried out with silica gel (230–400 mesh) as the stationary phase and pure solvents or various mixtures of solvents as the mobile phase. When autoflash was carried out, a Grace Reveleris instrument was used. The eluent composition is given for each compound. Mass spectra were obtained on a JEOL AccuTOF T100GC spectrometer. The instruments were operated in the DART/ESI+ mode at 10–15 eV.

Synthesis of propargylic alcohols **4** from **TEB**

All the propargylic alcohols, viz. 4,4,5,5-tetraethoxypent-2-yn-1-ol (**4a**), 5,5,6,6-tetraethoxy-hex-3-yn-2-ol (**4b**), 6,6,7,7-tetraethoxy-2-methylhept-4-yn-3-ol (**4c**), 1,1,2,2-tetraethoxyundec-3-yn-5-ol (**4d**), 5,5,6,6-tetraethoxy-2-methylhex-3-yn-2-ol (**4e**), 1-(3,3,4,4-tetraethoxybut-1-ynyl)cyclo-hexanol (**4f**), and 6,6,7,7-tetraethoxy-2-ethylhept-4-yn-3-ol (**4g**) were synthesized as described in the literature.^[2]

Syntheses of trimethylsilyl (TMS) ethers from **4**

5-Trimethylsiloxy-1,1,2,2-tetraethoxyundec-3-yne was prepared from **4d**. The alcohol (0.826 g, 2.40 mmol) was dissolved in dimethylformamide (DMF, 25 mL) under an N₂ atmosphere at rt. DMSO (0.045 g, 0.578 mmol) and triethylamine (TEA, 0.439 g, 4.34 mmol) were added and the mixture was stirred before trimethylchlorosilane (0.314 g, 2.89 mmol) was added dropwise over 5 min. The mixture was left stirring at rt for 3.5 h before it was quenched with water (25 mL). The phases were then separated, the aqueous phase was extracted with dichloromethane (DCM, 3 × 20 mL), and the organic extracts were combined and dried (MgSO₄). Filtration and evaporation of the solvent was followed by isolation by FC (mixture of hexanes). In order to reduce silica-induced decomposition of the product (desilylation) autoflash separation was applied; this gave the title compound (0.617 g, 79%) as a slightly brown liquid. IR (ATR): 2922 (s), 2853 (s), 1457 (m), 1377 (w), 1335 (w), 1250 (m), 1117 (s), 1079 (s), 1019 (m), 842 (s), 753 (w) cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 4.40 (t, *J* = 6.6 Hz, 1H), 4.36 (s, 1H), 3.65–3.78 (m, 8H), 1.17–1.70 (m, 22H), 0.86 (m, 3H), 0.16 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz): δ

104.4, 88.9, 64.8, 64.7, 62.8, 60.1, 38.7, 31.9, 29.1, 25.4, 22.8, 15.6, 15.5, 14.3, 0.31. HRMS calcd. for $C_{22}H_{44}O_5SiNa^+[M+Na]^+$ 439.6564804; found 439.38908.

5-Trimethylsiloxy-1,1,2,2-tetraethoxy-5-ethylhept-3-yne was prepared from **4g**. The alcohol (0.281 g, 0.885 mmol) was dissolved in DMF (22 mL) under N_2 atmosphere at rt. DMSO (0.016 g, 0.20 mmol) and TEA (0.135 g, 1.33 mmol) were added and the mixture was stirred, before trimethylchlorosilane (0.0961 g, 0.885 mmol) was added dropwise over 5 min. The mixture was left stirring at rt for 3 h before it was quenched with water (25 mL). The phases were then separated, the aqueous phase was extracted with DCM (3×15 mL), and the organic extracts were combined and dried ($MgSO_4$). Filtration and evaporation of the solvent was followed by isolation by FC (mixture of hexanes). In order to reduce silica-induced decomposition of the product (desilylation) autoflash separation was applied; this gave the title compound (0.288 g, 84%) as a slightly brown liquid. IR (ATR): 2974 (m), 2932 (w), 2881 (w), 2359 (w), 2340 (w), 1737 (w), 1457 (w), 1444 (w), 1388 (w), 1371 (w), 1324 (w), 1248 (m), 1150 (m), 1117 (s), 1058 (s), 1017 (s), 935 (w), 880 (m), 840 (s), 755 (m), 687 (w), 668 (w), 610 (w), 573 (w), 557 (w) cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz): δ 4.35 (s, 1H), 3.60–3.82 (m, 8H), 1.65 (q, $J=7.4$ Hz, 4H), 1.20 (m, 12H), 0.97 (t, $J=7.4$ Hz, 6H), 0.18 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 104.6, 99.08, 90.1, 80.1, 73.6, 64.5, 60.2, 35.6, 15.6, 15.5, 8.9, 2.0. HRMS calcd. for $C_{20}H_{40}O_5SiNa^+[M+Na]^+$ 411.60332; found 411.25433.

5-Trimethylsiloxy-1,1-diethoxy-5-ethylhept-3-yn-2-one (**6g**) was prepared in a two-step synthesis from **4g**, but without purifying the ketone formed in the first step. Alcohol **4g** (3.96 g, 11.5 mmol) was dissolved in a 7:3 mixture of THF and H_2O (120 mL). *p*-Toluene-sulfonic acid monohydrate (0.438 g, 2.30 mmol) was added and the mixture was refluxed for 4 h until the starting material was consumed (followed by TLC). Most of the THF was then evaporated on a rotary evaporator, before a saturated aqueous NaCl solution (30 mL) and DCM (30 mL) were added to the residue. The phases were separated and the aqueous phase was extracted with DCM (3×30 mL). The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$ (80 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. 1,1-Diethoxy-5-ethyl-5-hydroxyhept-3-yn-2-one (2.98 g, 93%) was obtained as a reddish liquid and appeared to be essentially pure according to 1H NMR [1H NMR ($CDCl_3$, 400 MHz): δ 4.68 (s, 1H), 3.54–3.68 (m, 4H), 1.68 (m, 4H), 1.20 (t, $J=7.0$ Hz, 12H), 0.99 (t, $J=7.0$ Hz, 6H)]. A sample of this ketone (0.2211 g, 0.885 mmol) was dissolved in DMF (22 mL) under N_2 atmosphere at rt. DMSO (0.016 g, 0.20 mmol) and TEA (0.135 g, 1.33 mmol) were added and the mixture was stirred, before trimethylchlorosilane (0.0961 g, 0.885 mmol) was added dropwise over 5 min. The mixture was left stirring at rt for 3 h before it was quenched with water (25 mL). The phases were then separated, the aqueous phase was extracted with DCM (3×15 mL), and the organic extracts were combined and dried ($MgSO_4$). Filtration and evaporation of the solvent was followed by isolation by FC (mixture of hexanes), yielding 1,1-diethoxy-5-ethyl-5-trimethylsiloxyhept-3-yn-2-one (0.288 g, 84%) as a light brown liquid. IR (ATR): 2976 (m), 2940 (w), 2881 (w), 2208 (w), 1687 (m), 1460 (w), 1374 (w), 1319 (w), 1250 (m), 1153 (m), 1059 (s), 1017 (s), 935 (w), 880 (m), 839 (s), 754 (m), 680 (w), 679 (w), 612 (w), 584 (w) cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz): δ 4.74 (s, 1H), 3.60–3.73 (m, 4H), 1.71 (q, $J=7.5$ Hz, 4H), 1.25 (t, $J=7.0$ Hz, 12H), 0.98 (t, $J=7.4$ Hz, 6H), 0.20 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 182.9, 101.6, 99.1, 83.1, 73.8, 63.1, 62.9, 53.6, 34.9, 15.3, 8.8, 8.6, 2.0, 1.7. HRMS calcd. for $C_{16}H_{30}O_4SiNa^+[M+Na]^+$ 337.4817204; found 337.181121.

Syntheses of *t*-butyldiphenylsilyl (TBDPs) ethers from **4**

Protection of primary and secondary propargylic alcohols: general procedure

Alcohol **4** was dissolved in anhydrous DMF under a N₂ atmosphere at rt. After addition of imidazole (3.0–5.0 equiv.) *t*-butyldiphenylsilyl chloride (TBDPSCl) (1.05–1.2 equiv.) was added dropwise at rt. The reaction mixture was stirred at rt until the starting material was consumed (monitored by TLC) and was then diluted with diethyl ether and washed with water and brine. The organic phase was subsequently dried (MgSO₄), filtered, and concentrated to provide a crude product from which silyl ether **5** was isolated by FC.

Protection of tertiary propargylic alcohols: general procedure

TBDPSCl (1.5 equiv.) was added dropwise to the mixture of propargylic alcohol **4** (1.0 equiv.), *N*-methylimidazole (2.6 mL/mmol), and I₂ (6.0 equiv.) at rt. The resulting mixture was stirred at 60 °C until the starting material was consumed (monitored by TLC) and extracted with diethyl ether (3 × 30 mL). The combined extracts were washed with aqueous saturated Na₂S₂O₃ solution and hydrochloric acid, dried (MgSO₄), filtered, and concentrated to give a crude product from which silyl ether **6** was isolated by FC.

Following these procedures, six silyl ether-protected alcohols were prepared.

1-*t*-Butyldiphenylsiloxy-4,4,5,5-tetraethoxy-pent-2-yne (**5a**) was synthesized from **4a** (2.75 g, 10.58 mmol) and TBDPSCl (3.49 g, 12.70 mmol). FC (10% hexanes in dichloromethane, *R_f* = 0.17) provided 4.95 g (94%) of the product as a colorless liquid. IR (ATR): 3072 (w), 3050 (w), 2974 (s), 2930 (s), 2893 (s), 2859 (s), 1962 (w), 1891 (w), 1827 (w), 1777 (w), 1589 (w), 1473 (m), 1462 (w), 1444 (w), 1428 (s), 1390 (m), 1371 (s), 1330 (w), 1246 (w), 1184 (s), 1107 (s), 1075 (s), 1018 (s), 998 (s), 962 (w), 938 (w), 877 (m), 823 (s), 789 (s), 739 (s), 701 (s), 690 (s) cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 7.73–7.70 (m, 4H), 7.44–7.35 (m, 6H), 4.43 (s, 2H), 4.37 (s, 1H), 3.83–3.66 (m, 8H), 1.23 (t, *J* = 7.1 Hz, 6H), 1.21 (t, *J* = 7.1 Hz, 6H), 1.05 (s, 9H); ¹³C NMR (CDCl₃, 101 MHz): δ 135.6 (4C), 133.1 (2C), 129.8 (2C), 127.7 (4C), 104.21 and 104.17 (1C, the two signals belong to two conformers), 98.7, 85.5, 79.5, 64.8, 52.80, 52.76, 26.63, 26.61 (2C), 19.2, 15.41, 15.40, 15.3 (2C). HRMS calcd. for C₂₉H₄₂O₅SiNa⁺ [*M* + Na]⁺ 521.26992; found 521.26974.

2-*t*-Butyldiphenylsiloxy-5,5,6,6-tetraethoxyhex-3-yne (**5b**) was synthesized from **4b** (7.42 g, 27.08 mmol) and TBDPSCl (7.82 g, 28.43 mmol). FC (5% methanol in hexanes, *R_f* = 0.30) provided 11.17 g (80%) of the product as a colorless liquid. IR (ATR): 3071 (w), 3049 (w), 2975 (s), 2930 (s), 2889 (s), 2858 (s), 1590 (w), 1473 (m), 1463 (w), 1443 (w), 1428 (s), 1390 (m), 1369 (m), 1338 (m), 1315 (m), 1242 (m), 1183 (s), 1103 (s), 1092 (s), 1075 (s), 1058 (s), 1016 (s), 984 (s), 937 (m), 922 (m), 869 (m), 823 (s), 762 (m), 739 (s), 700 (s), 689 (s), 622 (m), 613 (s), 535 (m) cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 7.77–7.67 (m, 4H), 7.44–7.35 (m, 6H), 4.56 (q, *J* = 6.5 Hz, 1H), 4.33 (s, 1H), 3.81–3.60 (m, 8H), 1.41 (d, *J* = 6.5 Hz, 3H), 1.23–1.15 (m, 12H), 1.06 (s, 9H); ¹³C NMR (CDCl₃, 101 MHz, CDCl₃) δ 136.0 (2C), 135.9 (2C), 133.8, 133.6, 129.8, 129.7, 127.7 (2C), 127.6 (2C), 104.32, 104.26, 98.6, 89.5, 78.2, 64.8, 64.74, 64.69, 64.63, 64.58, 60.2, 60.1, 60.03, 60.01, 26.92 (2C), 26.89, 25.2, 19.3, 15.55, 15.51, 15.49, 15.41. HRMS calcd. for C₃₀H₄₄O₅SiNa⁺ [*M* + Na]⁺ 535.28557; found 535.28577.

5-*t*-Butyldiphenylsiloxy-1,1,2,2-tetraethoxy-6-methylhept-3-yne (**5c**) was synthesized from **4c** (1.88 g, 6.23 mmol) and TBDPSCl (1.80 g, 6.54 mmol). FC (5% methanol in hexanes, *R_f* = 0.41) provided 2.83 g (84%) of the product as a colorless liquid. IR (ATR): 3072 (w), 3050 (w), 2973 (s), 2930 (s), 2894 (m), 2859 (m), 1958 (w), 1899 (w), 1824

(w), 1590 (w), 1472 (m), 1444 (w), 1428 (s), 1389 (m), 1367 (m), 1352 (m), 1332 (w), 1240 (w), 1186 (m), 1111 (s), 1106 (s), 1073 (s), 1028 (s), 1019 (s), 999 (s), 961 (w), 939 (m), 920 (w), 877 (w), 833 (s), 820 (s), 739 (s), 700 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 7.76–7.68 (m, 4H), 7.44–7.33 (m, 6H), 4.32 (d, $J = 4.6$ Hz, 1H), 4.28 (s, 1H), 3.78–3.54 (m, 8H), 1.91–1.83 (m, 1H), 1.22–1.11 (m, 12H), 1.08 (s, 9H), 1.05 (d, $J = 6.7$ Hz, 3H), 0.90 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 136.2 (2C), 136.0 (2C), 133.8, 133.7, 129.8, 129.6, 127.7 (2C), 127.5 (2C), 104.5, 98.8, 87.2, 80.0, 69.2, 64.5, 64.4, 60.4, 60.2, 35.4, 27.0 (3C), 19.5, 18.3, 17.1, 15.6, 15.5, 15.44, 15.42. HRMS calcd. for $\text{C}_{32}\text{H}_{48}\text{O}_5\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 563.31687; found 563.31670.

5-*t*-Butyldiphenylsiloxy-1,1,2,2-tetraethoxyundec-3-yne (**5d**) was synthesized from **4d** (0.37 g, 1.08 mmol) and TBDPSCl (0.36 g, 1.30 mmol). FC (5% methanol in hexanes, $R_f = 0.20$) provided 0.51 g (82%) of the product as a colorless liquid. The spectroscopic data were in agreement with those reported in the literature.^[2]

5-*t*-Butyldiphenylsiloxy-1,1,2,2-tetraethoxy-5-methylhex-3-yne (**5e**) was synthesized from **4e** (2.15 g, 7.47 mmol) and TBDPSCl (3.08 g, 11.21 mmol). FC (10% dichloromethane in hexanes, $R_f = 0.08$) provided 3.15 g (80%) of the product as a colorless liquid. IR (ATR): 3071 (w), 3050 (w), 2975 (s), 2931 (s), 2891 (m), 2858 (s), 1473 (w), 1444 (w), 1428 (m), 1388 (w), 1378 (w), 1361 (w), 1331 (w), 1251 (s), 1157 (s), 1108 (s), 1074 (s), 1043 (s), 956 (w), 937 (w), 893 (w), 821 (s), 740 (s), 700 (s), 609 (s), 554 (m) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 7.81–7.78 (m, 4H), 7.43–7.34 (m, 6H), 4.22 (s, 1H), 3.74–3.50 (m, 8H), 1.47 (s, 6H), 1.17 (t, $J = 7.1$ Hz, 6H), 1.10 (t, $J = 7.1$ Hz, 6H), 1.00 (s, 9H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 136.2 (4C), 135.2 (2C), 129.5 (2C), 127.5 (4C), 104.2, 98.4, 92.0, 77.6, 68.2, 64.5 (2C), 60.0 (2C), 32.7 (3C), 26.9 (2C), 19.3, 15.5 (2C), 15.4 (2C). HRMS calcd. for $\text{C}_{31}\text{H}_{46}\text{O}_5\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 549.30122; found 549.30145.

1-(1-*t*-Butyldiphenylsiloxy)cyclohexyl)-3,3,4,4-tetraethoxybut-1-yne (**5f**) was synthesized from **4f** (5.00 g, 15.24 mmol) and TBDPSCl (6.29 g, 22.86 mmol). FC (5% methanol in hexanes, $R_f = 0.38$) furnished 4.48 g (52%) of the product as a colorless liquid. IR (ATR): 3071 (w), 3048 (w), 2973 (s), 2931 (s), 2893 (s), 2856 (s), 1589 (w), 1473 (w), 1444 (w), 1427 (m), 1389 (w), 1362 (w), 1337 (w), 1291 (m), 1258 (w), 1232 (w), 1182 (m), 1103 (s), 1076 (s), 1018 (s), 1002 (s), 937 (m), 905 (m), 870 (s), 844 (w), 821 (s), 773 (w), 739 (s), 700 (s), 609 (s), 560 (w) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 7.80–7.78 (m, 4H), 7.42–7.32 (m, 6H), 4.16 (s, 1H), 3.69–3.50 (m, 4H), 3.45–3.34 (m, 4H), 1.91–1.88 (m, 2H), 1.63–1.44 (m, 7H), 1.23–1.11 (m, 1H), 1.14 (t, $J = 7.1$ Hz, 6H), 1.03 (t, $J = 7.1$ Hz, 6H), 1.01 (s, 9H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 136.3 (4C), 135.3 (2C), 129.4 (2C), 127.4 (4C), 104.4, 98.6, 90.7, 80.9, 71.5, 64.2 (2C), 60.2 (2C), 41.3 (2C), 27.1 (3C), 25.4, 23.3 (2C), 19.5, 15.5 (2C), 15.4 (2C). HRMS calcd. for $\text{C}_{34}\text{H}_{50}\text{O}_5\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 589.33277; found 589.33252.

Synthesis of TBDPS-protected ketones **6** from ketal **5**: General procedure

Siloxyated ketal **5** was dissolved in a 7:3 mixture of THF and H_2O , *p*-TsOH monohydrate (0.3–0.6 equiv.) was added, and the resulting mixture was refluxed until all the starting material had reacted (monitored with TLC). The reaction mixture was then mixed with an equal volume of CH_2Cl_2 and after shaking the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 \times), and the combined organic phases were dried (MgSO_4), filtered, and concentrated under reduced pressure to give a crude product, from

which siloxylated ketone **6** was isolated by FC. Using this procedure, the following six silyl-ether-protected ketones were prepared.

5-(*t*-Butyl)diphenylsiloxy-1,1-diethoxypent-3-yn-2-one (**6a**) was synthesized from **5a** (0.920 g, 1.84 mmol) and *p*-TsOH monohydrate (0.105 g, 0.55 mmol). The reaction mixture was refluxed for 8 h and FC purification (CH_2Cl_2 , $R_f = 0.40$) gave 0.440 g (56%) of the product as a colorless oil. IR (ATR): 3072 (w), 3050 (w), 2976 (w), 2960 (w), 2931 (m), 2893 (m), 2858 (m), 2212 (m), 1686 (s), 1589 (w), 1473 (w), 1463 (w), 1443 (w), 1428 (s), 1391 (w), 1369 (m), 1317 (w), 1250 (m), 1187 (w), 1159 (m), 1105 (s), 1086 (s), 1065 (s), 1008 (s), 998 (s), 965 (m), 939 (w), 906 (m), 823 (s), 782 (s), 739 (s), 700 (s), 690 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz): δ 7.71–7.69 (m, 4H), 7.46–7.38 (m, 6H), 4.71 (s, 1H), 4.48 (s, 2H), 3.74–3.59 (m, 4H), 1.26 (t, $J = 7.1$ Hz, 6H), 1.07 (s, 9H); ^{13}C NMR (CDCl_3 , 126 MHz): δ 182.5, 135.7 (4C), 132.6 (2C), 130.1 (2C), 128.0 (4C), 101.6, 94.0, 82.6, 63.1 (2C), 52.7, 26.7 (3C), 19.3, 15.2 (2C). HRMS calcd. for $\text{C}_{25}\text{H}_{32}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 5447.19675; found 447.19688.

5-(*t*-Butyl)diphenylsiloxy-1,1-diethoxylhex-3-yn-2-one (**6b**) was synthesized from **5b** (0.80 g, 1.56 mmol) and *p*-TsOH monohydrate (0.09 g, 0.46 mmol). The reaction mixture was refluxed for 12 h and FC purification (5% methanol in hexanes, $R_f = 0.33$) gave 0.55 g (81%) of the product as a colorless oil. IR (ATR): 3072 (w), 3049 (w), 2979 (m), 2962 (m), 2932 (m), 2889 (m), 2859 (m), 2214 (m), 1687 (s), 1589 (w), 1473 (m), 1463 (w), 1443 (w), 1428 (s), 1391 (m), 1370 (m), 1337 (m), 1312 (m), 1245 (m), 1187 (m), 1104 (s), 1094 (s), 1055 (s), 1008 (s), 998 (s), 980 (s), 937 (m), 921 (m), 887 (m), 822 (s), 760 (s), 739 (s), 700 (s), 690 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 7.76–7.67 (m, 4H), 7.45–7.36 (m, 6H), 4.67 (s, 1H), 4.60 (q, $J = 6.6$ Hz, 1H), 3.71–3.54 (m, 4H), 1.45 (d, $J = 6.6$ Hz, 3H), 1.24 (t, $J = 7.0$ Hz, 3H), 1.23 (t, $J = 7.0$ Hz, 3H), 1.08 (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 182.6, 136.0 (2C), 135.8 (2C), 133.1, 132.9, 130.04, 129.97, 127.8 (2C), 127.7 (2C), 101.3, 97.4, 81.2, 62.9, 62.8, 59.9, 26.8 (3C), 24.3, 19.2, 15.20, 15.19. HRMS calcd. for $\text{C}_{26}\text{H}_{34}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 461.21240; found 461.21266.

5-*t*-Butyldiphenylsiloxy-1,1-diethoxy-6-methylhept-3-yn-2-one (**6c**) was synthesized from **5c** (2.39 g, 4.42 mmol) and *p*-TsOH monohydrate (0.76 g, 4.0 mmol). The reaction mixture was refluxed for 16 h and FC purification (5% methanol in hexanes, $R_f = 0.45$) gave 2.06 g (100%) of the product as a colorless oil. IR (ATR): 3072 (w), 3050 (w), 2962 (s), 2931 (s), 2894 (m), 2859 (s), 2210 (m), 1962 (w), 1892 (w), 1686 (s), 1590 (w), 1568 (w), 1472 (s), 1446 (w), 1428 (s), 1389 (m), 1368 (m), 1362 (m), 1351 (m), 1332 (w), 1317 (w), 1244 (m), 1159 (m), 1105 (s), 1064 (s), 1007 (s), 998 (s), 961 (w), 938 (m), 904 (m), 821 (s), 740 (s), 700 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 7.74–7.67 (m, 4H), 7.46–7.35 (m, 6H), 4.60 (s, 1H), 4.33 (d, $J = 4.8$ Hz, 1H), 3.67–3.50 (m, 4H), 1.99–1.87 (m, 1H), 1.23 (t, $J = 7.0$ Hz, 3H), 1.21 (t, $J = 7.0$ Hz, 3H), 1.09 (s, 9H), 1.05 (d, $J = 6.7$ Hz, 3H), 0.92 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 182.6, 136.2 (2C), 136.0 (2C), 133.1 (2C), 130.1, 129.9, 127.8 (2C), 127.6 (2C), 101.2, 95.8, 83.1, 69.1, 62.8, 62.7, 35.2, 27.0 (3C), 19.5, 18.1, 17.3, 15.25, 15.23. HRMS calcd. for $\text{C}_{28}\text{H}_{38}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 489.24370; found 489.24381.

5-(*t*-Butyl)diphenylsiloxy-1,1-diethoxylundec-3-yn-2-one (**6d**) was synthesized from **5d** (0.77 g, 1.32 mmol) and *p*-TsOH monohydrate (0.15 g, 0.79 mmol). The reaction mixture was refluxed for 16 h and FC purification (CH_2Cl_2 , $R_f = 0.48$) gave 0.44 g (66%) of the product, a colorless oil, that shows spectroscopic data in accordance with the literature.^[2]

5-(*t*-Butyl)diphenylsiloxy-1,1-diethoxy-5-methylhex-3-yn-2-one (**6e**) was synthesized from **5e** (3.06 g, 5.81 mmol) and *p*-TsOH monohydrate (0.91 g, 4.80 mmol). The reaction mixture was refluxed for 24 h, and FC purification (5% methanol in hexanes, $R_f = 0.35$)

gave 2.47 g (94%) of the product as a colorless oil. IR (ATR): 3071 (w), 3049 (w), 2979 (s), 2932 (s), 2891 (s), 2858 (s), 2215 (m), 1689 (s), 1589 (w), 1472 (m), 1463 (m), 1445 (w), 1427 (s), 1380 (m), 1362 (m), 1319 (w), 1258 (s), 1238 (s), 1159 (s), 1104 (s), 1039 (s), 1003 (s), 953 (m), 940 (m), 919 (m), 869 (w), 821 (s), 795 (m), 741 (s), 700 (s), 609 (s), 559 (m), 531 (m); ^1H NMR (CDCl_3 , 400 MHz): δ 7.78–7.75 (m, 4H), 7.44–7.34 (m, 6H), 4.48 (s, 1H), 3.62–3.47 (m, 4H), 1.49 (s, 6H), 1.20 (t, $J = 7.1$ Hz, 6H), 1.04 (s, 9H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 182.5, 136.3 (4C), 134.5 (2C), 129.8 (2C), 127.6 (4C), 101.0, 99.6, 80.7, 67.9, 62.7 (2C), 32.0 (2C), 27.0 (3C), 19.3, 15.2 (2C). HRMS calcd. for $\text{C}_{27}\text{H}_{36}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 475.22805; found 475.22816.

4-(1-(*t*-Butyldiphenyl)siloxy)cyclohexyl)-1,1-diethoxybut-3-yn-2-one (**6f**) was synthesized from **6f** (3.69 g, 6.51 mmol) and *p*-TsOH monohydrate (1.48 g, 7.76 mmol). The reaction mixture was refluxed for 24 h and FC purification (hexanes and ethyl acetate, 95:5, $R_f = 0.46$) gave 2.35 g (73%) of the product as a colorless liquid. IR (ATR): 3070 (w), 3048 (w), 2932 (s), 2892 (m), 2857 (s), 2209 (m), 1687 (s), 1589 (w), 1472 (m), 1462 (m), 1445 (m), 1427 (s), 1390 (w), 1361 (w), 1339 (w), 1317 (w), 1289 (s), 1258 (w), 1232 (w), 1152 (m), 1095 (s), 1061 (s), 1023 (s), 999 (s), 936 (m), 905 (s), 867 (s), 821 (s), 739 (s), 700 (s), 610 (s), 544 (m) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 7.77–7.75 (m, 4H), 7.42–7.33 (m, 6H), 4.38 (s, 1H), 3.56–3.42 (m, 4H), 1.88–1.84 (m, 2H), 1.68–1.62 (m, 4H), 1.51–1.42 (m, 3H), 1.29–1.14 (m, 1H), 1.18 (t, $J = 7.0$ Hz, 6H), 1.05 (s, 9H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 182.3, 136.4 (4C), 134.7 (2C), 129.7 (2C), 127.5 (4C), 100.9, 98.9, 83.7, 71.2, 62.5 (2C), 40.5 (2C), 27.2 (3C), 25.1, 23.0 (2C), 19.5, 15.2 (2C). HRMS calcd. for $\text{C}_{30}\text{H}_{40}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 515.25935; found 515.25966.

Addition of diethylamine to ketones **6**: Formation of (Z)-4-(diethylamino)-1,1-diethoxyalk-3-en-2-ones (**7**)

(Z)-5-(*t*-Butyldiphenyl)siloxy-4-diethylamino-1,1-diethoxyhex-3-en-2-one (**7b**)

To a solution of 5-(*t*-butyl)diphenylsiloxy-1,1-diethoxyhex-3-yn-2-one (**6b**) (0.556 g, 1.27 mmol) in ethanol (25 mL) was added diethylamine (0.13 mL, 94 mg, 1.27 mmol) dropwise by a syringe. The mixture was stirred at rt until the starting material was consumed (2 h) (monitored by TLC). Ethanol was then evaporated on a rotary evaporator and a residue was obtained, which consisted of essentially pure **7b** (0.540 g, 83%). IR (ATR): 3070 (w), 3048 (w), 2970 (s), 2931 (s), 2857 (s), 1962 (w), 1892 (w), 1822 (w), 1731 (w), 1632 (s), 1590 (w), 1534 (s), 1484 (s), 1443 (s), 1427 (s), 1412 (s), 1381 (s), 1363 (s), 1313 (s), 1278 (s), 1164 (s), 1107 (s), 1077 (s), 1050 (s), 1007 (s), 959 (s), 890 (s), 819 (s), 795 (s), 739 (s), 699 (s), 663 (s), 606 (s), 577 (s) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ 7.67–7.57 (m, 4H), 7.42–7.28 (m, 6H), 6.81 (q, $J = 6.7$ Hz, 1H), 5.19 (s, 1H), 4.42 (s, 1H), 3.70 (q, $J = 7.0$ Hz, 2H), 3.60–3.38 (m, 6H), 1.34 (d, $J = 6.7$ Hz, 3H), 1.24–1.14 (m, 12H), 1.08 (s, 9H); ^{13}C NMR (126 MHz, CDCl_3): δ 189.5, 167.4, 135.9 (2C), 135.8 (2C), 134.0, 133.9, 129.7, 129.6, 127.6 (2C), 127.5 (2C), 103.9, 89.2, 66.4, 62.3, 62.2, 58.5 (2C), 27.3 (3C), 26.7, 22.4, 19.4, 18.5, 15.4, 15.3. HRMS calcd. for $\text{C}_{30}\text{H}_{46}\text{NO}_4\text{Si}^+ [\text{M} + \text{H}]^+$ 512.31961; found 512.31988.

(Z)-4-diethylamino-5-(*t*-butyldiphenyl)siloxy-1,1-diethoxy-6-methylhept-3-en-2-one (**7c**)

To a solution of ketone **6c** (0.574 g, 1.23 mmol) in ethanol (15 mL) was added diethylamine (0.13 mL, 94 mg, 1.27 mmol) dropwise by a syringe. The mixture was stirred at rt until the

starting material was consumed (2 h; monitored by TLC). Ethanol was evaporated on a rotary evaporator and a residue was obtained, from which pure **7c** (0.376 g, 57%) was isolated by FC (hexanes and ethyl acetate, 95:5; then CH₂Cl₂). IR (ATR): 3071 (w), 3048 (w), 2966 (s), 2930 (s), 2858 (s), 1740 (s), 1634 (m), 1589 (w), 1534 (s), 1462 (s), 1441 (s), 1428 (s), 1411 (m), 1384 (s), 1362 (s), 1322 (s), 1268 (s), 1240 (s), 1182 (m), 1156 (m), 1138 (m), 1104 (s), 1057 (s), 948 (m), 907 (s), 842 (s), 819 (s), 740 (s), 699 (s), 662 (s), 608 (s), 579 (s) cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ 7.68–7.57 (m, 4H), 7.41–7.28 (m, 6H), 6.55 (d, *J* = 9.7 Hz, 1H), 5.21 (s, 1H), 4.40 (s, 1H), 3.65–2.90 (m, 8H), 1.98–1.91 (m, 1H), 1.173 (t, *J* = 7.0 Hz, 3H), 1.166 (t, *J* = 7.0 Hz, 3H), 1.13 (seemingly t, *J* = 7.2 Hz, 6H), 1.06 (s, 9H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.78 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (CDCl₃, 126 MHz): δ 189.6, 164.5, 136.5 (2C), 136.3 (2C), 134.2, 133.7, 129.7, 129.5, 127.5 (2C), 127.2 (2C), 104.0, 91.8, 74.3, 62.1, 61.9, 60.5 (2C), 34.4, 27.5 (3C), 21.2, 20.8, 19.7, 18.1, 15.44, 15.40, 14.4. HRMS calcd. for C₃₂H₅₀NO₄Si⁺ [M + H]⁺ 540.35091; found 540.35098.

(Z)-4-diethylamino-5-trimethylsiloxy-1,1-diethoxy-5-ethylhept-3-en-2-one (7g)

Ketone **6g** (0.629 g, 2.02 mmol) was dissolved and stirred in EtOH (20 mL). Diethylamine (0.15 g, 2.0 mmol) was added dropwise by syringe and the mixture was stirred at rt for 2.5 h. EtOH was then thoroughly evaporated on a rotary evaporator and gave a yellowish residue, which was essentially pure **7g** (as judged from ¹H NMR and MS), in total 0.721 g (92%). IR (ATR): 2972 (m), 2933 (w), 2878 (w), 2208 (w), 1687 (m), 1460 (w), 1374 (w), 1319 (w), 1250 (m), 1153 (m), 1059 (s), 1017 (s), 935 (w), 880 (m), 839 (s), 754 (m), 680 (w), 679 (w), 612 (w), 584 (w) cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 5.50 (s, 1H), 4.60 (s, 1H), 3.50–3.70 (m, 8H), 1.88–1.92 (m, 2H), 1.68–2.74 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.2 Hz, 6H), 0.85 (t, *J* = 7.3 Hz, 6H), 0.16 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz): δ 100.5, 94.7, 84.9, 62.2, 47.1, 35.8, 15.5, 14.3, 9.0, 2.6. HRMS calcd. for C₁₆H₃₀O₄SiNa⁺ [M + Na]⁺ 387.62934; found 388.2805.

Cuprate addition to TBDPS-protected ketones 6: General procedure

CuI (1.0 equiv.) was dispersed into dry THF under N₂ and the resulting mixture was cooled to –30 °C before MeLi (2.0 equiv.) was added dropwise under stirring. When the addition was complete, the resulting mixture was left stirring at bath temperature for an additional 30 min before it was cooled to –78 °C. Ketone **6** (1.0 equiv.) in dry THF was added dropwise to the reaction mixture, which was stirred for another 60 min before a saturated aqueous solution of NH₄Cl was added in one portion. The hydrolysate was allowed to reach room temperature, the phases were separated, and the aqueous phase was extracted with diethyl ether (3 ×). The combined organic extracts were dried (MgSO₄), filtered, and concentrated under reduced pressure on a rotary evaporator to give the crude product, from which the *E* and *Z* isomers of the corresponding 5-substituted 5-(*t*-butyldiphenylsiloxy)-1,1-diethoxyalk-3-en-2-one (**8**) was isolated pure by FC. Using this procedure the following α,β-unsaturated alkenones were prepared.

5-(*t*-Butyl)diphenylsiloxy-1,1-diethoxy-4-methylpent-3-en-2-one (8a)

Ketone **6a** (2.01 g, 4.73 mmol) was reacted with Me₂CuLi and provided 2.27 g of a colorless crude product, which showed only one spot when analyzed by TLC (CH₂Cl₂, *R*_f = 0.22). The ¹H NMR spectrum of the residue was recorded and indicated that it mainly contained two products. Screening of solvents to find conditions that would allow separation of the

compounds was rather unsuccessful. In spite of this FC separation was attempted using 5% MeOH in hexanes as eluent and this gave essentially pure **8a** (0.82 g, 39%), which turned out to be a single isomer with *E* configuration (*vide supra*), and a small amount (0.15 g) of a sample that contained *E*-**8a** and another product. Repeated separation gave a very small amount of a pretty pure sample of the second product, which was given the structure 4-(*t*-butyl)diphenylsiloxy-5-diethoxy-3-methylcyclopent-2-enone (**9**).

Data for product mixture: IR (ATR): 3071 (m), 3049 (m), 2960 (s), 2931 (s), 2890 (s), 2858 (s), 1960 (w), 1893 (w), 1824 (w), 1714 (s), 1626 (s), 1589 (m), 1568 (w), 1472 (m), 1463 (m), 1428 (s), 1391 (m), 1372 (m), 1362 (m), 1315 (m), 1261 (w), 1227 (m), 1162 (s), 1103 (s), 1060 (s), 1007 (s), 998 (s), 938 (m), 908 (s), 873 (s), 854 (m), 822 (s), 740 (s), 700 (s) cm^{-1} .

Data for (*E*)-**8a**: IR (ATR): 3070 (w), 3049 (w), 2973 (s), 2960 (s), 2930 (s), 2889 (s), 2857 (s), 1696 (s), 1627 (s), 1590 (w), 1471 (m), 1443 (m), 1427 (s), 1391 (m), 1373 (m), 1316 (s), 1263 (w), 1231 (w), 1159 (s), 1105 (s), 1059 (s), 1008 (s), 978 (m), 894 (m), 852 (s), 821 (s), 740 (s), 700 (s), 612 (s) cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 7.68–7.66 (m, 4H), 7.45–7.37 (m, 6H), 7.02 (bs, 1H), 4.70 (s, 1H), 4.18 (s, 2H), 3.74–3.58 (m, 4H), 2.02 (s, 3H), 1.26 (t, $J = 7.1$ Hz, 6H), 1.10 (s, 9H); ^{13}C NMR (126 MHz, CDCl_3): δ 195.7, 159.4, 135.6 (4C), 133.2 (2C), 130.0 (2C), 127.93 (4C), 116.4, 102.7, 67.9, 62.8 (2C), 26.9, 19.4, 16.4, 15.34. HRMS calcd. for $\text{C}_{26}\text{H}_{36}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 463.22805; found 463.22812.

Data for **9**: ^1H NMR (500 MHz, CDCl_3): δ 7.76–7.74 (m, 2H), 7.68–7.66 (m, 2H), 7.47–7.36 (m, 6H), 5.85 (s, 1H), 4.66–4.65 (m, 1H), 3.95–3.89 (m, 2H), 3.18–3.11 (m, 1H), 1.93 (s, 3H), 1.12 (s, 9H), 0.97 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3): δ 203.2, 173.8, 136.3 (2C), 136.1 (2C), 133.4, 132.9, 130.2, 130.1, 129.2, 127.90 (2C), 127.7 (2C), 87.1, 78.7, 66.6, 27.1 (3C), 19.6, 16.7, 15.33. HRMS calcd. for $\text{C}_{24}\text{H}_{30}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 417.18619; found 417.18593.

5-(*t*-Butyldiphenylsiloxy)-1,1-diethoxy-4-methylhex-3-en-2-one (**8b**)

Ketone **6b** (1.53 g, 3.49 mmol) was reacted with Me_2CuLi to provide a colorless crude product, from which (*Z*)-**8b** (0.55 g, 35%) and (*E*)-**8b** (0.78 g, 49%) were isolated by FC (CH_2Cl_2 ; $R_{\text{f}(\text{Z})} = 0.34$, $R_{\text{f}(\text{E})} = 0.16$).

(*Z*)-**8b**: IR (ATR): 3071 (w), 3049 (w), 2975 (m), 2931 (m), 2888 (m), 2858 (m), 2360 (w), 1966 (w), 1890 (w), 1823 (w), 1773 (w), 1688 (s), 1615 (s), 1590 (w), 1472 (m), 1462 (w), 1443 (w), 1427 (s), 1390 (w), 1372 (m), 1362 (w), 1318 (w), 1240 (w), 1159 (m), 1107 (s), 1077 (s), 1058 (s), 1026 (s), 1008 (s), 996 (s), 951 (s), 905 (w), 892 (w), 852 (m), 822 (s), 739 (s), 700 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 7.65–7.56 (m, 4H), 7.42–7.28 (m, 6H), 6.21 (bs, 1H), 5.70 (q, $J = 6.3$ Hz, 1H), 4.46 (s, 1H), 3.62–3.42 (m, 4H), 2.04 (d, $J = 1.2$ Hz, 3H), 1.23–1.18 (m, 9H) 1.06 (s, 9H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 193.7, 167.2, 135.8 (2C), 135.7 (2C), 134.3, 134.0, 129.7, 129.6, 127.6 (2C), 127.5 (2C), 117.3, 102.6, 68.6, 62.8, 62.7, 27.1 (3C), 22.6, 19.8, 19.4, 15.3 (2C). HRMS calcd. for $\text{C}_{27}\text{H}_{38}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 477.24370; found 477.24375.

(*E*)-**8b**: IR (ATR): 3071 (w), 3049 (w), 2976 (s), 2931 (s), 2888 (m), 2858 (s), 1959 (w), 1893 (w), 1827 (w), 1777 (w), 1694 (s), 1622 (s), 1590 (w), 1473 (m), 1462 (w), 1444 (w), 1427 (s), 1391 (m), 1372 (s), 1318 (m), 1292 (w), 1229 (w), 1166 (s), 1110 (s), 1058 (s), 1008 (s), 998 (s), 964 (s), 939 (m), 895 (m), 872 (m), 822 (s), 778 (s), 739 (s), 700 (s), 689 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71–7.61 (m, 4H), 7.45–7.31 (m, 6H), 6.73 (bs, 1H), 4.62 (s, 1H), 4.22 (q, $J = 6.3$ Hz, 1H), 3.71–3.52 (m, 4H), 2.06 (d, $J = 0.9$ Hz, 3H),

1.23 (t, $J = 7.1$ Hz, 6H), 1.17 (d, $J = 6.4$ Hz, 3H), 1.10 (s, 9H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 195.9, 164.0, 135.89 (2C), 135.87 (2C), 134.1, 133.4, 129.8 (2C), 127.68 (2C), 127.66 (2C), 116.8, 102.6, 74.1, 62.7, 62.6, 27.0 (3C), 22.9, 19.3, 16.2, 15.3 (2C). HRMS calcd. for $\text{C}_{27}\text{H}_{38}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 477.24370; found 477.24375.

5-(*t*-Butyldiphenyl)siloxy-1,1-diethoxy-4,6-dimethylhept-3-en-2-one (8c)

Ketone (**6c**) (1.80 g, 3.86 mmol) was reacted with Me_2CuLi to provide a colorless crude product, from which (*Z*)-**8c** (0.77 g, 41%) and (*E*)-**8c** (1.03 g, 55%) were separated by FC (CH_2Cl_2 ; $R_{\text{f}(\text{Z})} = 0.45$, $R_{\text{f}(\text{E})} = 0.24$).

(*Z*)-**8c**: IR (ATR): 3072 (w), 3049 (w), 2962 (s), 2931 (s), 2890 (m), 2873 (m), 2858 (s), 2358 (w), 1964 (w), 1889 (w), 1824 (w), 1765 (w), 1693 (s), 1615 (s), 1471 (s), 1445 (m), 1427 (s), 1387 (s), 1372 (s), 1317 (m), 1275 (w), 1159 (m), 1104 (s), 1057 (s), 1007 (s), 999 (s), 960 (m), 939 (s), 908 (w), 891 (w), 860 (s), 821 (s), 739 (s), 700 (s) cm^{-1} ; ^1H NMR (CHCl_3 , 400 MHz): δ 7.67–7.58 (m, 4H), 7.41–7.28 (m, 6H), 6.19 (bs, 1H), 5.57 (d, $J = 7.1$ Hz, 1H), 4.41 (s, 1H), 3.62–3.41 (m, 4H), 1.89 (d, $J = 1.1$ Hz, 3H), 1.84–1.76 (m, 1H), 1.210 (t, $J = 7.1$ Hz, 3H), 1.205 (t, $J = 7.1$ Hz, 3H), 1.09 (s, 9H), 0.87 (d, $J = 6.7$ Hz, 3H), 0.74 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 193.6, 164.1, 136.20 (2C), 136.15 (2C), 134.26, 134.25, 129.57, 129.56, 127.5 (2C), 127.4 (2C), 120.2, 102.6, 75.7, 62.8, 62.6, 34.4, 27.3 (3C), 20.4, 19.8, 19.2, 18.7, 15.3 (2C). HRMS calcd. for $\text{C}_{29}\text{H}_{42}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 505.27500; found 505.27518.

(*E*)-**8c**: IR (ATR): 3072 (w), 3049 (w), 2961 (s), 2931 (s), 2892 (m), 2858 (s), 2355 (w), 1965 (w), 1891 (w), 1825 (w), 1776 (w), 1695 (s), 1619 (s), 1590 (w), 1471 (m), 1446 (w), 1427 (s), 1390 (m), 1367 (m), 1317 (w), 1262 (w), 1227 (w), 1160 (m), 1104 (s), 1057 (s), 1007 (s), 999 (s), 937 (w), 893 (w), 875 (m), 838 (m), 821 (s), 739 (s), 700 (s), 691 (s) cm^{-1} ; ^1H NMR (CHCl_3 , 400 MHz): δ 7.69–7.58 (m, 4H), 7.44–7.29 (m, 6H), 6.36 (d, $J = 0.9$ Hz, 1H), 4.52 (s, 1H), 3.84 (d, $J = 6.0$ Hz, 1H), 3.64–3.45 (m, 4H), 2.02 (d, $J = 1.2$ Hz, 3H), 1.85–1.77 (m, 1H), 1.203 (t, $J = 7.0$ Hz, 3H), 1.196 (t, $J = 7.0$ Hz, 3H), 1.08 (s, 9H), 0.84 (d, $J = 6.7$ Hz, 3H), 0.69 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (CHCl_3 , 100 MHz): δ 195.2, 161.5, 136.24 (2C), 136.19 (2C), 134.0, 133.7, 129.7 (2C), 127.6 (2C), 127.5 (2C), 119.8, 102.5, 83.8, 62.6, 62.5, 33.0, 27.2 (3C), 19.7, 19.1, 18.4, 16.7, 15.3 (2C). HRMS calcd. for $\text{C}_{29}\text{H}_{42}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 505.27500; found 505.27512.

5-(*t*-Butyldiphenyl)siloxy-1,1-diethoxy-4-methylundec-3-en-2-one (8d)

Ketone **6d** (0.56 g, 1.10 mmol) was reacted with Me_2CuLi and provided a yellowish crude product, from which (*Z*)-**8d** (0.26 g, 45%) and (*E*)-**8d** (0.28 g, 48%) were separated by FC (CH_2Cl_2 ; $R_{\text{f}(\text{Z})} = 0.62$, $R_{\text{f}(\text{E})} = 0.35$). The spectroscopic data are in agreement with the literature.^[2]

5-(*t*-Butyldiphenyl)siloxy-1,1-diethoxy-4,5-dimethylhex-3-en-2-one (8e)

Ketone **6e** (1.37 g, 3.02 mmol) was reacted with Me_2CuLi and gave a yellowish crude product, from which (*Z*)-**8e** (0.38 g, 27%) and (*E*)-**8e** (1.04 g, 73%) were separated by FC (CH_2Cl_2 ; $R_{\text{f}(\text{Z})} = 0.44$; $R_{\text{f}(\text{E})} = 0.23$).

(*Z*)-**8e**: IR (ATR): 3071 (w), 3049 (w), 3015 (w), 2976 (s), 2931 (s), 2887 (m), 2857 (s), 2219 (w), 1961 (w), 1892 (w), 1826 (w), 1776 (w), 1692 (s), 1597 (s), 1472 (m), 1463 (m), 1441 (m), 1427 (s), 1385 (m), 1371 (w), 1360 (m), 1316 (m), 1237 (w), 1156 (s), 1128 (m), 1103 (s), 1058 (s), 1039 (s), 1026 (s), 1006 (s), 999 (s), 937 (m), 916 (m), 893 (m), 849 (m), 821 (s), 792 (m), 773 (m), 740 (s), 700 (s), 678 (s) cm^{-1} ; ^1H NMR (CHCl_3 ,

400 MHz): δ 7.71 (dd, $J_1 = 6.8$ Hz, $J_2 = 0.6$ Hz, 4H), 7.42–7.34 (m, 6H), 6.33 (s, 1H), 4.51 (s, 1H), 3.69–3.49 (m, 4H), 2.26 (bs, 3H), 1.43 (s, 6H), 1.22 (t, $J = 7.1$, 6H), 1.04 (s, 9H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 194.1, 170.5, 136.3 (4C), 135.7 (2C), 129.6 (2C), 127.5 (4C), 117.3, 103.6, 79.5, 63.2 (2C), 28.0, 27.5 (3C), 26.2 (2C), 19.7, 15.3 (2C). HRMS calcd. for $\text{C}_{28}\text{H}_{40}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 491.25935; found 491.25944.

(*E*)-**8e**: IR (ATR): 3071 (w), 3049 (w), 2977 (s), 2931 (s), 2887 (m), 2857 (s), 1965 (w), 1898 (w), 1826 (w), 1780 (w), 1694 (s), 1616 (s), 1590 (m), 1568 (w), 1472 (m), 1463 (m), 1444 (m), 1427 (s), 1384 (s), 1361 (s), 1316 (m), 1249 (s), 1171 (s), 1103 (s), 1044 (s), 1028 (s), 1007 (s), 999 (s), 935 (m), 912 (m), 900 (m), 878 (m), 821 (s), 770 (m), 741 (s), 701 (s), 684 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz): δ 7.75–7.73 (m, 4H), 7.43–7.34 (m, 6H), 7.07 (bs, 1H), 4.67 (s, 1H), 3.72–3.56 (m, 4H), 2.17 (d, $J = 1.0$, 3H), 1.226 (s, 6H), 1.225 (t, $J = 7.1$ Hz, 6H), 1.07 (s, 9H); ^{13}C NMR (CDCl_3 , 126 MHz): δ 196.7, 166.7, 136.2 (4C), 135.4 (2C), 129.6 (2C), 127.6 (4C), 116.2, 102.8, 78.2, 62.7 (2C), 28.6, 27.4 (3C), 19.6, 16.3 (2C), 15.4 (2C). HRMS calcd. for $\text{C}_{28}\text{H}_{40}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 491.25935; found 491.25944.

4-[[1-(*t*-Butyl)diphenylsiloxy]cyclohex]-1,1-diethoxyl-4-methylbut-3-en-2-one (**8f**)

Ketone **6f** (2.52 g, 5.11 mmol) was reacted with Me_2CuLi and gave a yellowish crude product, from which (*Z*)-**8f** (0.29 g, 11%) and (*E*)-**8f** (1.64 g, 63%) were separated by FC (CH_2Cl_2 ; $R_f(\text{Z}) = 0.45$, $R_f(\text{E}) = 0.27$).

(*Z*)-**8f**: IR (ATR): 3071 (w), 3048 (w), 2930 (m), 2892 (m), 2856 (m), 2212 (w), 1961 (w), 1896 (w), 1830 (w), 1699 (s), 1590 (m), 1473 (m), 1446 (m), 1427 (s), 1389 (w), 1371 (w), 1360 (w), 1315 (w), 1281 (w), 1258 (w), 1226 (w), 1139 (m), 1103 (s), 1059 (s), 1027 (s), 999 (s), 931 (m), 902 (m), 877 (m), 846 (w), 821 (s), 740 (s), 700 (s), 689 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 7.77–7.74 (m, 4H), 7.41–7.31 (m, 6H), 6.00 (d, $J = 1.2$ Hz, 1H), 4.57 (s, 1H), 3.70–3.50 (m, 4H), 2.03–1.98 (m, 2H), 1.75 (d, $J = 1.1$ Hz, 3H), 1.67–1.50 (m, 4H), 1.35–1.16 (m, 1H), 1.23 (t, $J = 7.0$ Hz, 9H), 1.03 (s, 9H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 196.1, 155.8, 136.4 (4C), 135.7 (2C), 129.4 (2C), 127.3 (4C), 123.1, 103.3, 79.0, 63.3 (2C), 37.8 (2C), 27.4 (3C), 25.4, 24.4, 23.1 (2C), 20.1, 15.3 (2C). HRMS calcd. for $\text{C}_{31}\text{H}_{44}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 531.29065; found 531.29081.

(*E*)-**8f**: IR (ATR): 3071 (w), 3048 (w), 2930 (s), 2892 (m), 2856 (s), 2143 (w), 1966 (w), 1897 (w), 1825 (w), 1775 (w), 1696 (s), 1613 (s), 1473 (w), 1446 (m), 1427 (s), 1388 (w), 1360 (w), 1344 (w), 1317 (w), 1295 (m), 1259 (w), 1215 (w), 1169 (m), 1137 (m), 1003 (s), 1059 (s), 1024 (s), 998 (s), 933 (w), 900 (s), 888 (s), 857 (w), 821 (s), 740 (s), 700 (s), 689 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71–7.69 (m, 4H), 7.41–7.31 (m, 6H), 6.31 (s, 1H), 4.49 (s, 1H), 3.66–3.49 (m, 4H), 2.12 (bs, 3H), 1.98–1.95 (m, 2H), 1.65–1.58 (m, 4H), 1.40–1.37 (m, 1H), 1.28–1.10 (m, 3H), 1.22 (t, $J = 7.1$ Hz, 6H), 0.99 (s, 9H); ^{13}C NMR (CDCl_3 , 101 MHz): δ 195.8, 161.2, 136.2 (4C), 135.3 (2C), 129.5 (2C), 127.4 (4C), 119.2, 102.4, 79.1, 62.6 (2C), 37.2 (2C), 27.2 (3C), 25.7, 23.5 (2C), 19.8, 16.0, 15.3 (2C). HRMS calcd. for $\text{C}_{31}\text{H}_{44}\text{O}_4\text{SiNa}^+ [\text{M} + \text{Na}]^+$ 531.29065; found 531.29082.

Addition of 1,3-propanedithiol to 5-(*t*-butyl)diphenylsiloxy-1,1-diethoxyhex-3-yn-2-one (**6b**): Formation of 3-(2-(1-(*t*-butyl)diphenylsiloxyethyl)-1,3-dithian-2-yl)-1,1-diethoxy-Propan-2-one (**10b**)

1,3-Propanedithiol (0.186 g, 1.72 mmol) in dry THF (10 mL) was treated with NaOMe (0.109 g, 2.02 mol) at rt, and to the resulting mixture, which was cooled to -78°C and

stirred, was added a THF solution of 5-(*t*-butyl)diphenylsiloxy-1,1-diethoxylhex-3-yn-2-one (**6b**) (0.680 g, 1.55 mmol in 10 mL) over 15 min. The reaction mixture was stirred for 17.5 h and allowed to reach rt. The reaction was quenched with a saturated aqueous solution of NH₄Cl (40 mL), and the mixture was extracted with DCM (3 × 50 mL), dried (MgSO₄), filtered, and concentrated to provide a crude product from which **10b** (0.691 g, 82%) was isolated as colorless liquid by FC (10% ethyl acetate in hexanes, *R_f* = 0.21). IR (ATR): 3070 (w), 3047 (w), 2973 (s), 2929 (s), 2892 (s), 2855 (s), 1729 (s), 1589 (w), 1472 (m), 1442 (m), 1426 (s), 1390 (s), 1373 (s), 1313 (s), 1277 (m), 1240 (s), 1132 (s), 1103 (s), 1057 (s), 1004 (s), 971 (s), 957 (s), 908 (s), 871 (m), 821 (s), 740 (s), 701 (s), 609 (s) cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.79–7.75 (m, 4H), 7.44–7.36 (m, 6H), 4.68 (s, 1H), 4.62 (q, *J* = 6.3 Hz, 1H), 3.74–3.54 (m, 6H), 2.95–2.84 (m, 2H), 2.74–2.69 (m, 1H), 2.59–2.54 (m, 1H), 2.02–1.95 (m, 1H), 1.86–1.78 (m, 1H), 1.27–1.23 (m, 9H), 1.03 (s, 9H); ¹³C NMR (126 MHz, CDCl₃): δ 202.2, 136.2 (4C), 134.8, 133.3, 129.8, 129.5, 127.7 (2C), 127.4 (2C), 103.3, 73.6, 63.5, 63.3, 42.0, 27.1 (3C), 26.7, 26.2, 25.9, 24.9, 19.7, 19.2, 15.34, 15.30. HRMS calcd for C₂₉H₄₂O₄SiNa⁺ [*M* + Na]⁺ 569.21915; found 569.21938.

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References

- [1] (a) Bol'shedvorskaya, R. L.; Vereshchagin, L. I. *Russ. Chem. Rev.* **1973**, *42*, 225–240; (b) Posner, G. H. *Org. React.* **1972**, *19*, 1–113 (c) Kozlowski, J. A.; Trost, B. M.; Fleming, I. (Eds.); *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, UK, 1991; vol. 4, ch. 1.4; (c) Tomioka, K. *Synthesis* **1990**, 541–549; (d) Sengee, M.; Sydnes, L. K. *Synthesis* **2011**, 3899–3907.
- [2] Sydnes, L. K.; Holmelid, B.; Sengee, M.; Hanstein, M. *J. Org. Chem.* **2009**, *74*, 3430–3443.
- [3] (a) Sydnes, L. K.; Isanov, R.; Sengee, M.; Livi, F. *Synth. Commun.* **2013**, *43*, 2898–2905; (b) Nes, I.; Sydnes, L. K. *Synthesis* **2015**, *47*, 89–94.
- [4] Erdenebileg, U.; Høstmark, I.; Polden, K.; Sydnes, L. K. *J. Org. Chem.* **2014**, *79*, 1213–1221.
- [5] (a) Gaunt, M. J.; Sneddon, H. F.; Hewitt, P. R.; Orsini, P.; Hook, D. F.; Ley, S. V. *Org. Biomol. Chem.* **2003**, *1*, 15–16; (b) Sneddon, H. F.; Gaunt, M. J.; Ley, S. V. *Org. Lett.* **2003**, *5*, 1147–1150; (a) Valdernesnes, S.; Apeland, I.; Flemmen, G.; Sydnes, L. K. *Helv. Chim. Acta* **2012**, *95*, 2099–2122.
- [6] (a) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon Press: Oxford, 1992 (b) Bergmann, E. D.; Ginsburg, D.; Pappo, R. *Org. React.* **1959**, *10*, 182–542; (b) Rossiter, B. E.; Swingle, N. M. *Chem. Rev.* **1992**, *92*, 771–806.
- [7] Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley & Sons: New York, 1991; ch. 2, pp. 10–143.
- [8] Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley & Sons: New York, 1991; pp. 68–87.
- [9] Kvernenes, O. H.; Sydnes, L. K. *Org. Synth.* **2005**, *83*, 184.

- [10] Sydnnes, L. K.; Holmelid, B.; Kvernenes, O. H.; Sandberg, M.; Hodne, M.; Bakstad, E. *Tetrahedron* **2007**, *63*, 4144.
- [11] Visser, R. G.; Bos, H. J. T.; Brandsma, L. *Rec. Trav. Chim. Pays-Bas* **1980**, *99*, 70.
- [12] (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley & Sons: New York, 1991; pp. 178–198 (b) Holmelid, B.; Kvernenes, O. H.; Hodne, M.; Sydnnes, L. K. *Arkivoc* **2008**, *6*, 26–41; (c) Sydnnes, L. K.; Holmelid, B.; Kvernenes, O. H.; Valdersnes, S.; Hodne, M.; Boman, K. *Arkivoc* **2008**, *14*, 242–268.
- [13] Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley & Sons: New York, 1991; pp. 77–83.
- [14] Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon Press: Oxford, UK, 1969; pp. 316–328.
- [15] (a) Gilman, H.; Jones, R. G.; Woods, L. A. *J. Am. Chem. Soc.* **1952**, *74*, 1630 (b) Jones, R. G.; Gilman, H. *Chem. Rev.* **1954**, *54*, 847; (c) House, H. O.; Respass, W. L.; Whitsides, G. M. *J. Org. Chem.* **1966**, *31*, 3128; (d) Taylor, R. K. *Organocopper Reagents*; Oxford University Press: Oxford, UK, 1994.
- [16] Posner, G. H. *Organic Reactions* **1972**, *19*, 1–114.
- [17] (a) Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851; (b) Siddall, J. B.; Biskup, M.; Fried, J. H. *J. Am. Chem. Soc.* **1966**, *91*, 1853; (c) Klein, J.; Turkel, R. M. *J. Am. Chem. Soc.* **1969**, *91*, 6186.
- [18] (a) Jackman, L. M.; Wiley, R. H. *J. Chem. Soc.* **1960**, 2881; (b) Douglas, A. W.; Goldstein, J. H. *J. Mol. Spec.* **1965**, *16*, 1; (c) Bothner-By, A. A.; Naar-Colin, C. *J. Am. Chem. Soc.* **1961**, *83*, 231 (d) Barfield, M.; Spear, R. J.; Sternhell, S. *Chem. Rev.* **1976**, *76*, 593; (e) Sydnnes, L. K.; Hemmingsen, T. H. *Acta Chem. Scand. B* **1985**, *39*, 93.
- [19] (a) Bellamy, L. J. *The Infrared Spectra of Complex Molecules*, 3rd ed.; Chapman and Hall: London, UK, 1975/1978; ch. 9; (b) Jones, R. N.; Humpries, P.; Dobriner, K. *J. Am. Chem. Soc.* **1950**, *72*, 956; (c) Fuson, N.; Josien, M. L.; Shelton, E. M. *J. Am. Chem. Soc.* **1954**, *76*, 2526.
- [20] (a) Stothers, J. B. *Carbon-13 NMR Spectroscopy*; Academic Press: New York, 1972; pp. 289–294 (b) Barton, D. H. R.; Hulshof, L. A. *J. Chem. Soc., Perkin Trans. I* **1977**, 1103; (c) Klunder, A. J. H.; Zwanenburg, B. *Tetrahedron Lett.* **1981**, *22*, 4557; (d) Malmström, J.; Christophersen, C.; Barrero, A. F.; Oltra, J. E.; Justicia, J.; Rosales, A. *J. Nat. Prod.* **2002**, *65*, 364; (e) Blanco-Urgoiti, J.; Abdi, D.; Domínguez, G.; Pérez-Castells, J. *Tetrahedron* **2008**, *64*, 67.
- [21] (a) Ghribi, A.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1984**, *25*, 3083; (b) Normant, J. F.; Alexakis, A.; Ghribi, A. *Tetrahedron* **1989**, *45*, 507.
- [22] Bali, A. K.; Sunnam, S. K.; Prasad, K. R. *Org. Lett.* **2014**, *16*, 4001.