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A Straightforward Synthesis of Substituted Cyclopentenones

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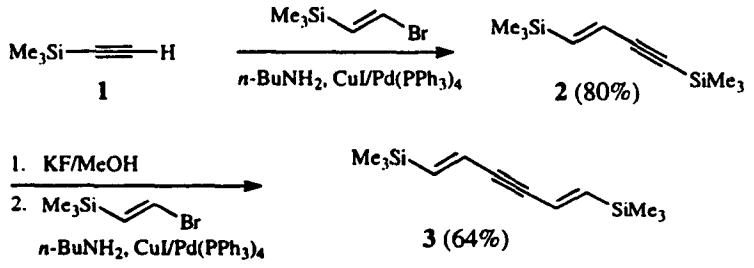
Abstract: A new synthetic approach to substituted silylated cyclopentenones has been developed, starting from an easily accessible bis-silylated conjugated dienyne and based upon the reactions with unsaturated acyl chlorides. Copyright © 1996 Elsevier Science Ltd

In recent papers[1] we have reported that (all *E*) 1,4-bis-trimethylsilyl-1,3-diene and 1,6-bis-trimethylsilyl-1,3,5-triene can undergo a chemoselective and sequential electrophilic substitution of the trimethylsilyl group with acyl chlorides in the presence of $AlCl_3$. The sequence of reactions proved to be very useful for the ready synthesis of a series of natural compounds having a conjugated polyene structure[2].

In connection with this type of synthetic work, we considered of interest to extend this approach to other bis-silylated systems presenting different type of unsaturations, which could be considered as possible useful building blocks for the construction of other polyunsaturated natural compounds.

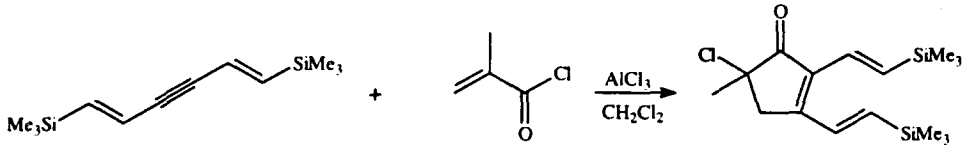
With this in mind we have developed the synthesis of (*E*,*E*)-1,6-bis(trimethylsilyl)-hexa-1,5-dien-3-yne **3**, which has been easily obtained according to the Scheme 1:

Scheme 1



The reaction of commercial trimethylsilylacetylene **1** with *E*-1-bromo-2-trimethylsilylethene in the presence of a Pd(0) catalyst[3] leads to *E*-1,4-bis(trimethylsilyl)-1-buten-3-yne[4] **2** in 80% yield. After appropriate desilylation, the resulting enyne is subjected to a further coupling reaction with the same halovinylsilane, leading to the desired compound **3**[5] in 64% yield.

Thus, we have explored the possibility of a chemoselective substitution of the trimethylsilyl groups with acyl chlorides. With this aim we have employed the α,β-unsaturated acyl chloride **4**, and, according to our procedure[1], we have performed the reaction in methylene chloride by adding a solution of the complex methacryloyl chloride-$AlCl_3$ at -10° C to the dienyne **3** in CH_2Cl_2. Surprisingly, as a result we have not observed the formation of the expected mono-substituted silyl ketone, but the formation of a different product (21% yield, purified by flash chromatography) which, after appropriate analysis (GC/MS, ^{1}H-NMR and ^{13}C-NMR), revealed to be a substituted cyclopentenone **7**[5], according to the equation:



3 **4** **7**

This result prompted us to further investigate the reaction and, in the first instance, we have attempted to increase the yield modifying the reaction conditions, *i.e.* Lewis acid, solvent and mode of addition (Table 1). Aluminium chloride seemed to be the most suitable reagent (no reaction was observed with $SnCl_4$[6] and $AgBF_4$[6,7], frequently used in reactions of unsaturated acyl chlorides with vinylsilanes). We have also changed the mode of addition (procedure **B** in Table 1), by adding a solution of the methacryloyl chloride to the mixture of $AlCl_3$ and dienyne **3** in methylene chloride without any relevant improvement of the yield. With 1,2-dichloroethane as solvent the reaction proceeded but with the same low yield obtained in CH_2Cl_2 (25%). Finally, when we have added the dienyne **3** to the solution of the complex methacryloyl chloride-$AlCl_3$ in methylene chloride at -10° C (procedure **C** in Table 1) we have obtained a relevant improvement of the yield.

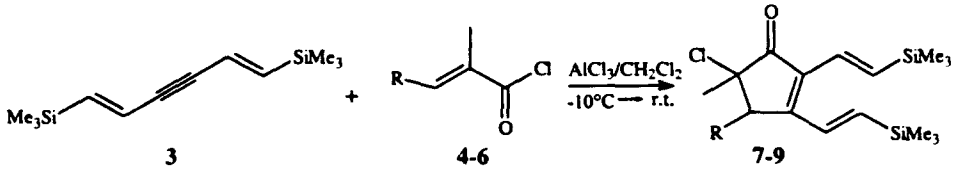
This procedure was extended to a few other α,β-unsaturated acyl chlorides. Compound **8**[5] (a 3:2 mixture of diastereomers) was obtained in 81% yield from 2,3-dimethylacryloyl chloride (42% with procedure **B**), whereas compound **9**[5] was obtained in 53% yield.

The following procedure for the synthesis of compound **7** is representative.

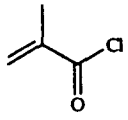
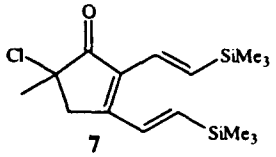
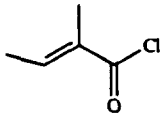
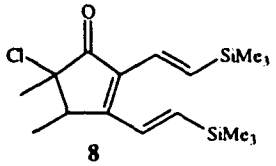
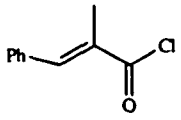
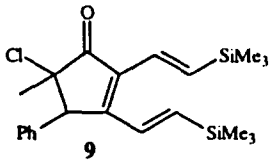
A CH_2Cl_2 (10 mL) solution of **3** (0.40 g, 1.80 mmol) was added, under nitrogen, to a solution of the complex acyl chloride-$AlCl_3$, previously prepared by adding methacryloyl chloride (0.21 mL, 2.16 mmol) to a cold, -10° C, stirred suspension of $AlCl_3$ (0.29 g, 2.16 mmol) in CH_2Cl_2 (10 mL). After complete addition, the reaction mixture was slowly brought at room temperature, stirred for 5 h, the time required for completion, quenched with saturated aqueous NH_4Cl, and extracted with ethyl acetate. The organic extracts were washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, petroleum ether/ethyl acetate 9.8/0.2) leading to 0.34 g (58% yield) of the product **7**[5].

It is notheworthy that several examples are reported in the literature regarding the reactions of vinylsilanes with α,β-unsaturated acyl chlorides and leading to cyclic compounds[6-8], but, to our knowledge, this reaction represents the first example of a simple cyclization, deriving from a preliminary addition of the acyclic acyl chloride to the triple bond and followed by a subsequent ring closure, leading to substituted cyclopentenones. Moreover, these compounds could be considered useful intermediates for prostaglandin synthesis, due to the presence of several functionalities on the substrates.

Table 1. Reactions of dienyne 3 with unsaturated acyl chlorides



3 4-6 7-9

Acyl Chlorides	Procedures	Products	Yield(%)[a]
 4	A	 7	21
4	B	7	23
4	B[b]	7	25
4	C	7	58
 5	B	 8	42
5	C	8	81
 6	C	 9	53

[a]Yields refer to products purified by flash chromatography. [b]Reaction performed in 1,2-dichloroethane.

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5. ^{1}H-NMR data were measured at 500 MHz on a Bruker AM 500, and ^{13}C-NMR data at 125.8 MHz. GC/mass-spectrometry analysis were performed on a Hewlett-Packard 5890A GC equipped with HP-1 capillary column, 25 m, and HP MSD 5970B. **(1*E*,5*E*)-1,6-bis(trimethylsilyl)-1,5-hexadien-3-yne 3**, ^{1}H-NMR data: δ 0.08 (s, 18H), 6.04 (d, *J* = 18.7 Hz, 2H), 6.41 (d, *J* = 18.7 Hz, 2H) ppm. MS m/e 222 (M^+, 6), 207 (18), 149 (9), 133 (14), 123 (13), 73 (100), 59 (31), 45 (26), 43 (22). **2,3-di(*E*-2-trimethylsilylethenyl)-5-chloro-5-methyl-2-cyclopentenone 7**, ^{1}H-NMR data: δ 0.12 (s, 9H), 0.16 (s, 9H), 1.67 (s, 3H), 2.98 (d, *J* = 18.7 Hz, 1H), 3.21 (d, *J* = 18.7 Hz, 1H), 6.56 (d, *J* = 18.9 Hz, 1H), 6.77 (d, *J* = 19.2 Hz, 1H), 7.05 (d, *J* = 19.2 Hz, 1H), 7.25 (d, *J* = 18.9 Hz, 1H) ppm. MS m/e 328 (M+2, 4) 326 (M^+, 9), 311 (16), 291 (82), 218 (80), 203 (43), 167 (11), 145 (11), 129 (13), 93 (21), 73 (100), 59 (19), 45 (27). ^{13}C-NMR data: δ -1.70, -1.59, 26.71, 44.30, 64.46, 131.05, 131.15, 136.16, 139.62, 143.27, 159.04, 202.36 ppm. **2,3-di(*E*-2-trimethylsilylethenyl)-5-chloro-4,5-dimethyl-2-cyclopentenone 8**, (the diastereomers were separated by flash chromatography with petroleum ether as eluent), ^{1}H-NMR data (major diastereomer): δ 0.12 (s, 9H), 0.17 (s, 9H), 1.13 (d, *J* = 7.3 Hz, 3H), 1.61 (s, 3H), 3.48 (q, *J* = 7.3 Hz, 1H), 6.56 (d, *J* = 19.2 Hz, 1H), 6.75 (d, *J* = 19.2 Hz, 1H), 7.02 (d, *J* = 19.2 Hz, 1H), 7.13 (d, *J* = 19.2 Hz, 1H) ppm; (minor diastereomer) δ 0.11 (s, 9H), 0.16 (s, 9H), 1.26 (d, *J* = 7.1 Hz, 3H), 1.63 (s, 3H), 3.10 (q, *J* = 7.1 Hz, 1H), 6.57 (d, *J* = 19.2 Hz, 1H), 6.72 (d, *J* = 19.2 Hz, 1H), 7.01 (d, *J* = 19.2 Hz, 1H), 7.12 (d, *J* = 19.2 Hz, 1H) ppm. MS m/e 342 (M+2, 2), 340 (M^+, 4), 325 (12), 305 (55), 232 (45), 217 (47), 201 (11), 167 (8), 159 (7), 143 (9), 93 (11), 73 (100), 59 (12), 45 (20). **2,3-di(*E*-2-trimethylsilylethenyl)-4-phenyl-5-chloro-5-methyl-2-cyclopentenone 9**, ^{1}H-NMR data: δ 0.16 (s, 9H), 0.18 (s, 9H), 1.67 (s, 3H), 5.34 (s, 1H), 6.80 (d, *J* = 19.2 Hz, 1H), 6.81 (d, *J* = 19.2 Hz, 1H), 7.10 (d, *J* = 19.2 Hz, 1H), 7.19 (d, *J* = 19.2 Hz, 1H), 7.21-7.35 (m, 5H) ppm. MS m/e 367 (19), 351(19), 293 (17), 263 (7), 73 (100), 59 (5), 45 (15).
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