

A New Approach to Silylated Ketones and Dicarboxyl Compounds with a Conjugated (all *E*) Diene or Triene Structure

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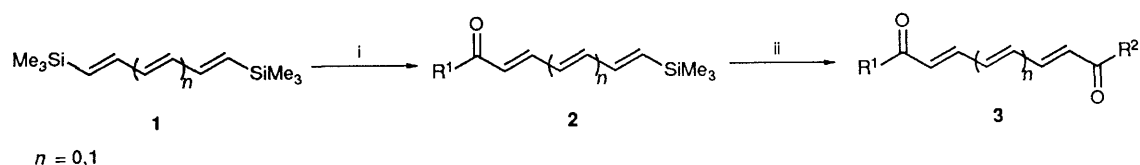
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Silylated ketones and dicarboxyl compounds with a conjugated diene or triene structure are obtained by electrophilic substitution reactions between (1*E*,3*E*)-1,4-bis(trimethylsilyl)buta-1,3-diene or (1*E*,3*E*,5*E*)-1,6-bis(trimethylsilyl)hexa-1,3,5-triene and acyl chlorides in the presence of aluminium trichloride.

In the last decade unsaturated organosilicon compounds have been extensively studied because of their interesting potential in selective organic synthesis.¹ Thus vinyl² and dienyl silanes³ have received much attention and their synthetic utility has been used in numerous carbon-carbon bond forming reactions. However, the use of the latter compounds has been mainly restricted to Diels-Alder reactions,^{1*b*,3*d*} whereas examples of electrophilic substitution, which are rather

common with vinyl silanes,^{1*a-e*,2*a,c,d*} are rare with dienyl silanes.^{3*e*} In the course of our previous studies on the synthesis of stereodefined alkene systems,⁴ we have devised a route to 1-silylated dienes with an *E-E* or *E-Z* configuration.⁵ Now we report a new synthetic approach to all *E* silylated ketones and dicarboxyl compounds with a conjugated diene or triene structure.

As depicted in Scheme 1, the crucial step of our procedure



Scheme 1 Reagents and conditions: i, $R^1\text{COCl-AlCl}_3$, CH_2Cl_2 , $0\text{ }^\circ\text{C}$; ii, $R^2\text{COCl-AlCl}_3$, CH_2Cl_2 , $0\text{ }^\circ\text{C}$ to room temp.

Table 1 Substitution products **2** and **3** from the reaction of compounds **1** with acyl chlorides in the presence of aluminium trichloride^a

Entry substrate 1 ($n = 0, 1$)	$R^1\text{COCl}$	$R^2\text{COCl}$	Product 2 ^{b, d} yield (%)	Product 3 ^{c, e} overall yield (%)	Time / h
1 ($n = 0$)	PhCOCl	—		—	1.0
2 ($n = 0$)	PhCOCl	$\text{Me}(\text{CH}_2)_6\text{COCl}$	—		17.0
3 ($n = 0$)	$\text{MeO}_2\text{C}(\text{CH}_2)_3\text{COCl}$	—		—	1.0
4 ($n = 0$)	$\text{MeO}_2\text{C}(\text{CH}_2)_3\text{COCl}$	MeCOCl	—		37.0
5 ($n = 1$)	$\text{Me}(\text{CH}_2)_2\text{COCl}$	—		—	1.0
6 ($n = 1$)	$\text{Me}(\text{CH}_2)_2\text{COCl}$	PhCH ₂ COCl	—		3.0
7 ($n = 1$)	$\text{MeO}_2\text{C}(\text{CH}_2)_6\text{COCl}$	—		—	0.5
8 ($n = 1$)	$\text{MeO}_2\text{C}(\text{CH}_2)_8\text{COCl}$	$\text{Me}(\text{CH}_2)_2\text{COCl}$	—		8.5
9 ($n = 1$)	$\text{Me}(\text{CH}_2)_6\text{COCl}$	—		—	1.0
10 ($n = 1$)	$\text{Me}(\text{CH}_2)_6\text{COCl}$	PhCOCl	—		16.0

^a For reaction conditions see text. ^b Yields refer to products purified by distillation. ^c Overall yields of products isolated by flash chromatography and purified by crystallization. ^d All these new compounds were fully characterized by MS, IR, ^1H and ^{13}C NMR spectroscopy. ^e All these new compounds were fully characterized by IR, ^1H and ^{13}C NMR spectroscopy.

involves the highly chemoselective substitution of a trimethylsilyl group of the readily available compounds **1**, (1*E*,3*E*)-1,4-bis(trimethylsilyl)buta-1,3-diene ($n = 0$),^{3d,6} or (1*E*,3*E*,5*E*)-1,6-bis(trimethylsilyl)hexa-1,3,5-triene ($n = 1$),[†] with acyl chlorides in the presence of aluminium trichloride to obtain silylated ketones **2**. Substitution of the second silyl group leads to the diketones **3**. As far as the first step is concerned, it is worth noting that compounds **1**, in spite of the higher number of double bonds between the two silyl groups, behave in a manner similar to (*E*)-1,2-bis(trimethylsilyl)ethene in which monoacylation has been obtained^{2e} with a variety of acyl chlorides and aluminium trichloride.

In particular, we have found that in order to obtain various silylated ketones **2**, it was sufficient to react the substrate **1** with equimolar amounts of acyl chloride and AlCl₃ at 0 °C in CH₂Cl₂ under a nitrogen atmosphere. Only monosubstitution products were obtained, with high retention of configuration (stereoisomeric purities $\geq 98\%$), which were isolated in good yields by simple distillation. Moreover, the preparation of the dicarbonyl compounds **3** was carried out by a one-pot procedure, by just adding the other acyl chloride after completion of the first step, without isolation of the mono-substitution product.

The following procedure for the synthesis of methyl (11*E*,13*E*,15*E*)-16-trimethylsilyl-10-oxohexadeca-11,13,15-trienoate **2** (Table 1, entry 7) and of methyl (11*E*,13*E*,15*E*)-10,17-dioxoicosa-11,13,15-trienoate **3** (Table 1, entry 8) is representative. A CH₂Cl₂ solution (8 ml) of freshly distilled methyl 10-chloro-10-oxodecanoate (1.17 g, 5.0 mmol) was added, under nitrogen, to a cold (0 °C), stirred suspension of anhydrous AlCl₃ (1.32 g, 10 mmol) in CH₂Cl₂ (7 ml). (It is noteworthy that when functionalised acyl chlorides were used in the first step, a molar ratio of AlCl₃ to acyl chloride of 2 : 1 allowed the use of shorter reaction times and led to higher yields of monosubstitution products, whereas, in the other cases, it was sufficient to use a molar ratio of AlCl₃ to acyl chloride of 1 : 1). The resulting mixture was stirred at 0 °C for 10 min and the clear solution obtained was transferred *via* syringe to the addition funnel of a three-necked flask, equipped with a magnetic stirrer and cooled at 0 °C, under nitrogen, which contained a CH₂Cl₂ solution (10 ml) of (1*E*,3*E*,5*E*)-1,6-bis(trimethylsilyl)hexa-1,3,5-triene **1** ($n = 1$) (1 g, 4.5 mmol). After complete addition at 0 °C, the mixture was stirred at the same temperature and the reaction was monitored by GLC analysis (fused silica capillary column SE 30, 30 m). After reaction completion (0.5 h), the mixture was quenched with saturated aqueous NH₄Cl and extracted with ether. The combined organic extracts were washed with water, dried over Na₂SO₄ and concentrated. The residue was purified by distillation to give 1.02 g (65% yield) of methyl (11*E*,13*E*,15*E*)-16-trimethylsilyl-10-oxohexadeca-11,13,15-trienoate (b.p. 170–172 °C, 9×10^{-5} mbar). The product was characterized by GC-mass-spectrometric analysis and the stereochemistry of the double bonds was ascertained from the ¹H NMR coupling constants between the vinylic protons.[‡]

In order to prepare the dicarbonyl derivative (Table 1, entry 8), the first step was carried out as described above. Then a solution of the butyryl chloride–aluminium trichloride complex [prepared as described above from 0.71 g (6.7 mmol) of butyryl chloride and 0.88 g (6.7 mmol) of AlCl₃] was dropped at 0 °C under nitrogen into the reaction mixture resulting from the completion of the first step. After the addition, the mixture was slowly brought to room temperature and stirred for 8 h. The same work-up procedure afforded a crude residue, which was flash chromatographed on silica gel (eluent CH₂Cl₂–Et₂O, 9.5 : 0.5). Crystallization from EtOH afforded 0.80 g of pure methyl (11*E*,13*E*,15*E*)-10,17-dioxoicosa-

11,13,15-trienoate (m.p. 118–119 °C).[‡] The overall yield, based upon the starting triene **1** was 52%.

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[‡] Selected spectroscopic data: (2*E*,4*E*)-1-phenyl-5-trimethylsilylpenta-2,4-dien-1-one (entry 1): ¹H NMR (200 MHz, CDCl₃) δ 0.13 (s, 9H), 6.46 (d, *J* 18.2 Hz, 1H), 6.77 (dd, *J* 18.2, 10.3 Hz, 1H), 6.95 (d, *J* 15.0 Hz, 1H), 7.35 (dd, *J* 15.0, 10.3 Hz, 1H), 7.40–7.60 (m, 3H), 7.88–8.00 (m, 2H); ¹³C NMR (50.3 MHz, CDCl₃) δ –1.58, 125.60, 128.42, 128.57, 132.72, 138.05, 141.89, 146.33, 146.87, 191.09; IR (KBr) ν 1662, 1015, 864, 840 cm^{–1}; MS (70 eV): *m/z* (%) 230 (10, M⁺), 215 (100), 157 (26), 141 (91), 115 (19), 105 (40), 77 (46), 73 (25).

(2*E*,4*E*)-1-phenyl-trideca-2,4-diene-1,6-dione (entry 2): ¹H NMR (200 MHz, CDCl₃) δ 0.86 (br. s, 3H), 1.27 (br. s, 8H), 1.59–1.66 (m, 2H), 2.60 (t, *J* 7.0 Hz, 2H), 6.53 (d, *J* 15.2 Hz, 1H), 7.20–7.65 (m, 6H), 7.90–8.01 (m, 2H); ¹³C NMR (50.3 MHz, CDCl₃) δ 14.08, 22.60, 24.03, 29.07, 29.18, 31.66, 41.55, 128.53, 128.78, 132.20, 133.33, 136.20, 137.33, 138.73, 141.16, 189.69, 200.23; IR (KBr) ν 1688, 1657, 1023 cm^{–1}.

Methyl (11*E*,13*E*,15*E*)-16-trimethylsilyl-10-oxohexadeca-11,13,15-trienoate (entry 7): ¹H NMR (200 MHz, CDCl₃) δ 0.07 (s, 9H), 1.26 (br. s, 8H), 1.54–1.60 (m, 4H), 2.26 (t, *J* 7.3 Hz, 2H), 2.51 (t, *J* 7.2 Hz, 2H), 3.63 (s, 3H), 6.11 (d, *J* 17.5 Hz, 1H), 6.15 (d, *J* 15.5 Hz, 1H), 6.20–6.38 (m, 1H), 6.46–6.66 (m, 2H), 7.15 (dd, *J* 15.5, 10.9 Hz, 1H); ¹³C NMR (50.3 MHz, CDCl₃) δ –1.48, 24.33, 24.89, 29.06, 29.21, 34.06, 40.69, 51.46, 129.95, 130.66, 140.62, 142.11, 142.85, 143.47, 174.32, 200.73; IR (KBr) ν 1739, 1677, 1600, 1017, 867, 841 cm^{–1}; MS (70 eV): *m/z* (%) 350 (7, M⁺), 335 (6), 319 (4), 277 (4), 251 (8), 207 (16), 194 (28), 179 (26), 73 (100).

Methyl (11*E*,13*E*,15*E*)-10,17-dioxoicosa-11,13,15-trienoate (entry 8): ¹H NMR (200 MHz, CDCl₃) δ 0.91 (t, *J* 7.3 Hz, 3H), 1.27 (br. s, 8H), 1.50–1.70 (m, 6H), 2.26 (t, *J* 7.3 Hz, 2H), 2.53 (t, *J* 7.1 Hz, 4H), 3.63 (s, 3H), 6.27 (d, *J* 15.4 Hz, 2H), 6.52–6.75 (m, 2H), 7.17 (ddd, *J* 15.4, 7.1, 2.9 Hz, 2H); ¹³C NMR (50.3 MHz, CDCl₃) δ 13.79, 17.64, 24.14, 24.89, 29.05, 29.18, 34.06, 41.14, 43.04, 51.46, 132.17, 132.21, 138.22, 138.25, 140.22, 174.30, 200.34, 200.40; IR (KBr) ν 1731, 1684, 1602, 1034 cm^{–1}.

[†] (1*E*,3*E*,5*E*)-1,6-bis(trimethylsilyl)hexa-1,3,5-triene was prepared by our procedure⁵ using *E*-2-trimethylsilyl ethenylmagnesium bromide as a reagent in both cross-coupling steps. Details of the preparation will be given elsewhere.