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An easy approach to 1-silylated ketones and asymmetrical 1,6- and 1,8-dicarbonyl compounds

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Abstract

A variety of 1-silylated ketones and asymmetrical 1,6- and 1,8-dicarbonyl compounds are synthesized with 70–85% yields by means of Pd-catalysed selective hydrogenation reactions of the corresponding unsaturated conjugated products, readily available by a previously reported procedure.

1. Introduction

In continuation of our studies on the synthesis of stereodefined olefinic systems [1,2] we have recently devised a new synthetic approach to silylated ketones and dicarbonyl compounds with a conjugated (all *E*) diene or triene structure, based upon the chemoselective and sequential substitution of the trimethylsilyl groups [3] of conjugated dienyl and trienyl disilyl derivatives **1** with acyl chlorides [4] (Scheme 1).

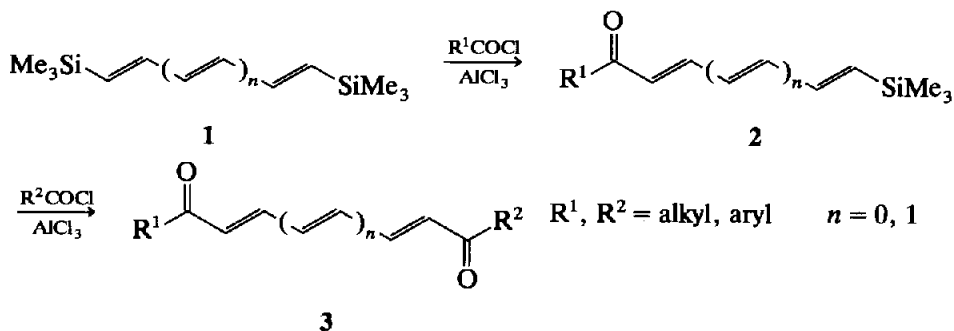
We have successfully applied the method to the one-pot synthesis of a natural product, ostopanic acid [5], a plant anticancer agent and to the synthesis of both the (6*E*) isomer and a structural analogue of

leukotriene B₃ [5]. Furthermore, more recently we have extended the same methodology to the synthesis of tetraene compounds of special interest, such as the methyl ester of β -parinaric acid [6], an interesting fluorescence probe for biological membranes.

To illustrate further the versatility and the very useful synthetic application of our procedure, we now report the synthesis of a series of aliphatic 1-silylated ketones [7,8], which are potential precursors of organo-functional siloxanes [8], and of 1,6- and 1,8-dicarbonyl compounds, which are important compounds in organic synthesis [9].

Although a number of methods have been reported for the synthesis of 1,6- and 1,8-dicarbonyl compounds [10], most of these methods have several disadvantages with respect to convenience or efficiency. Therefore, we evaluated the preparation of the above compounds

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Scheme 1.

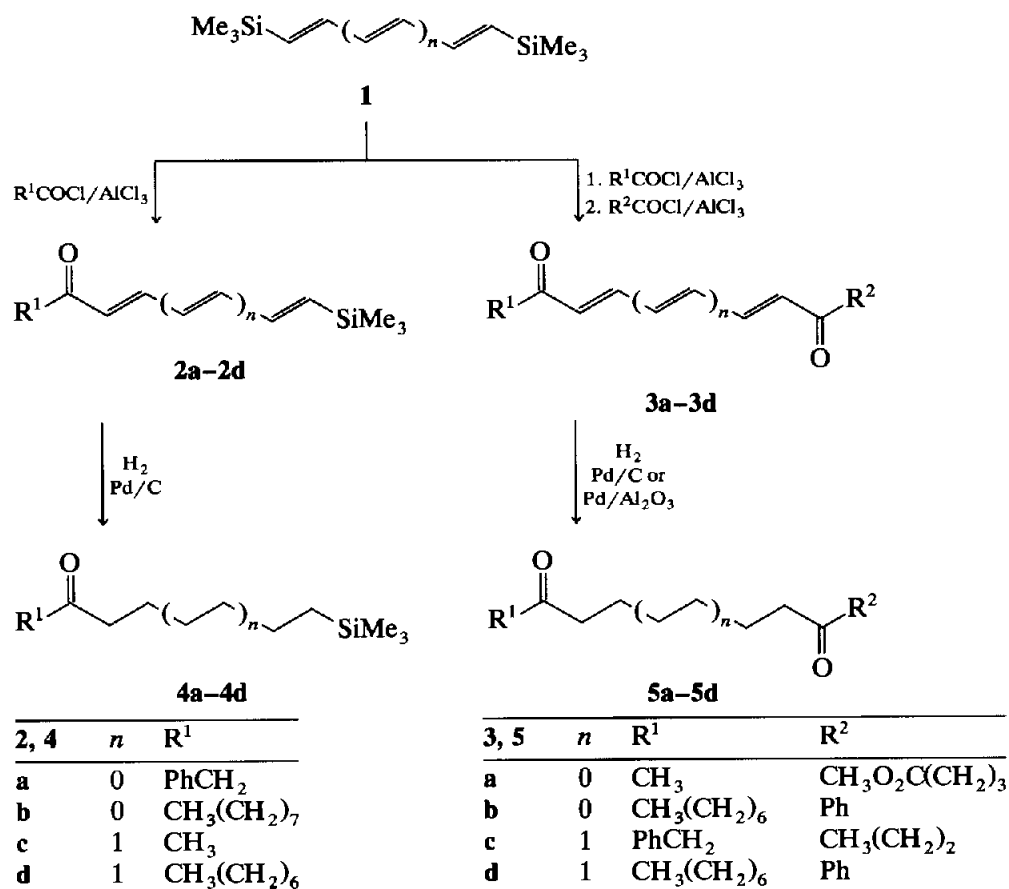
by selective reduction of the double bonds of the polyenes, which can be easily obtained from the disilyl derivatives **1**. There are several examples of organic reduction [11], which is still a challenging and demanding topic in synthetic chemistry, particularly for compounds with several reducible moieties [12]. An astute choice of reducing agent and catalyst often can lead to sufficient selectivity for practical synthesis without resorting to complex systems, such as silicon hydrides in the presence of Pd(0) and ZnCl₂ [13], carbonylferrates [14] or [(PPh₃)CuH]₆ [15], usually employed in the selective reduction of the olefinic bond of α,β unsaturated carbonyl compounds. We looked for a heterogeneous system that could operate satisfactorily.

2. Results

Previous results [16] using Cu- and Pd-supported catalysts in the selective hydrogenation suggested the use of these metals, but the choice of the catalyst is critical. Indeed, while some preliminary hydrogenation

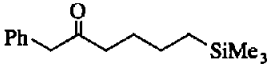
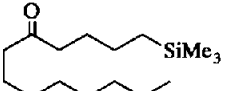
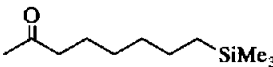
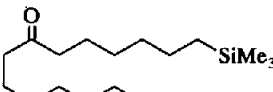
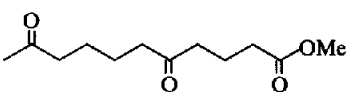
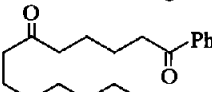
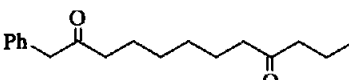
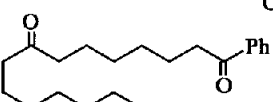
reactions promoted by Cu/Al₂O₃ gave very unsatisfactory results, good results were obtained with Pd-supported catalysts. The synthetic sequence is depicted in Scheme 2.

When unsaturated ketosilanes with a conjugated (all *E*) diene (**2a** or **2b**) or triene (**2c** or **2d**) structure were allowed to react with molecular hydrogen in methylene chloride at room temperature in the presence of a catalytic amount of 5% Pd on C, 1-silylated ketones **4a–4d** were easily isolated in 70–85% yields (Table 1). When we performed the reduction reactions of compounds **3a–3d** under the same conditions and with the same catalyst, a lack of selectivity was observed in the case of compounds **3b** and **3d** which both have an aromatic R² group. The product obtained from conjugate reduction of the dienone system **3b** or trienone **3d** showed that hydrogenolysis [11,17] of the carbonyl group α to the aromatic ring to methylene had occurred. This undesirable side overreduction was completely suppressed by conducting the reactions in the presence of a milder catalyst, such as Pd/Al₂O₃ (1%),



Scheme 2.

TABLE 1. 1-Silylated ketones 4a–4d and diketones 5a–5d prepared

Product	Reaction time (h)	Yield ^a	Kugelrohr oven temp (°C)/mbar or m.p. (°C) ^b (solvent)	MS (70 eV) ^c m/z (%)
4a 	0.8	83	120/2.5 × 10 ⁻⁴	233 (4), 157 (17), 91 (22), 75 (20), 73 (100), 59 (7), 55 (6)
4b 	0.7	85	125/3 × 10 ⁻⁴	255 (4), 185 (6), 157 (11), 130 (14), 114 (8), 75 (41), 73 (100), 59 (9), 57 (10), 55 (14), 45 (12), 43 (23)
4c 	5	82	70/3 × 10 ⁻⁴	185 (14), 143 (52), 115 (10), 75 (90), 73 (100), 45 (22), 43 (59)
4d 	1	70	150/2.5 × 10 ⁻⁴	269 (2), 227 (6), 185 (3), 157 (3), 143 (12), 130 (14), 127 (5), 95 (10), 75 (87), 73 (100), 57 (26), 45 (15), 43 (27)
5a 	3	75	225/2.5 × 10 ⁻⁴	197 (2), 170 (7), 144 (19), 129 (20), 112 (23), 101 (30), 84 (16), 81 (37), 59 (36), 55 (35), 43 (100)
5b 	2	80	46–47 (petroleum ether)	270 (1), 204 (15), 168 (16), 146 (33), 143 (29), 133 (9), 127 (9), 120 (44), 105 (100), 77 (42), 57 (24)
5c 	4	77	185/2 × 10 ⁻⁴	274 (M ⁺ , 1), 183 (14), 137 (19), 95 (12), 91 (43), 81 (16), 71 (100), 55 (20), 43 (63)
5d 	3	72	47–48 (petroleum ether)	298 (2), 232 (5), 217 (3), 175 (27), 171 (11), 133 (10), 120 (50), 105 (100), 77 (34), 57 (25)

^a Yield of pure isolated product. Satisfactory microanalyses obtained: C ± 0.28, H ± 0.25. ^b Melting points are determined with a Kofler apparatus and are uncorrected. ^c Taken with a GC/MS apparatus: Hewlett-Packard 5970 mass selective detector, MSD, and 5890 gas chromatograph, equipped with a Supelco SPB-1 30 m capillary column.

and the corresponding dicarbonyl compounds 5 were then synthesized in 72–80% yields (Table 1).

In conclusion, the simplicity of the process, the ready availability of the reagents, the use of relatively inexpensive Pd catalysts, the high yields of reduced products and the very simple and convenient experimental procedure are clear advantages of this reduction. Moreover, although the reactions have been carried out on a 1 mmol scale, the process can be scaled up without difficulty.

3. Experimental details

All the unsaturated silylated ketones 2a–2d and diketones 3a–3d were prepared according to our previously reported procedure [4]. Hydrogen was of ultra-high purity grade. Pd/C (5%) was purchased from

Engelhard. Pd/γ-Al₂O₃ (1%), purchased from Girdler (G 129), was reduced at 200°C for 3 h in an H₂ stream, washed with water until chloride free and dried overnight at 90°C. Reagent quality CH₂Cl₂ was used without further purification. All reactions were performed at room temperature. The reaction products were purified by distillation with a Kugelrohr apparatus or by crystallization. The purified reaction products were identified by microanalysis, mass spectra, IR spectra, and ¹H NMR and ¹³C nuclear magnetic resonance (NMR) spectra. NMR spectral data taken in CDCl₃ used the residual CHCl₃ singlet at δ 7.26 as the standard for ¹H data and the triplet centred at δ 77.0 as the standard for ¹³C spectra.

Immediately before use, the catalyst samples were subjected to a pretreatment procedure as follows: Pd/C (5%) was dried at 50°C for 20 min, whereas Pd/Al₂O₃ (1%) was kept under H₂ flow at 200°C for 5 min.

3.1. 1-Silylated ketones 4: general procedure

A solution of compound **2** (1 mmol) in CH_2Cl_2 (6 ml) was added under H_2 at room temperature into the reaction vessel where the catalyst (Pd/C, 100 mg) had been previously pretreated. The final pressure of H_2 was adjusted to 1 atm with a mercury levelling bulb, stirring commenced and the H_2 uptake was measured with a mercury-sealed gas burette. Absorption of hydrogen stopped after the calculated molar amounts were taken up, in the time reported in Table 1, and the catalyst was removed by filtration. The solvent was evaporated under reduced pressure and the crude product **4** was purified by distillation with a Kugelrohr apparatus to provide an analytically pure sample (Table 2).

3.2. Dicarbonyl compounds 5: general procedure

The procedure for the synthesis of products **5a–5d** is the same as that reported for the ketones **4a–4d** but

Pd/ Al_2O_3 (150 mg) is the catalyst employed in the reduction of compounds **3b** and **3d** (Table 2).

Acknowledgment

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TABLE 2. Spectral data of compounds **4a–4d** and **5a–5d**

Product	IR ^a ν (cm^{-1})	¹ H NMR (CDCl_3) ^b δ (ppm), <i>J</i> (Hz)	¹³ C NMR (CDCl_3) ^b δ (ppm)
4a	1710 (vs), 1245 (m), 860 (vs), 835 (vs), 770 (m)	−0.04 (s, 9H), 0.38–0.53 (m, 2H), 1.15–1.32 (m, 2H), 1.45–1.68 (m, 2H), 2.45 (t, 2H, <i>J</i> = 7.3), 3.68 (s, 2H), 7.15–7.45 (m, 5H _{arom})	−1.76 (Me ₃ Si), 16.44 (C ₁), 23.50, 27.52 (C ₂ , C ₃), 41.70 (C ₄), 50.14 (C ₆), 126.91, 128.65, 129.36, 134.33 (Ph), 208.67 (C ₅)
4b	1710 (vs), 1250 (m), 860 (vs), 840 (vs), 745 (m)	−0.11 (s, 9H), 0.35–0.50 (m, 2H), 0.75–0.85 (m, 3H), 1.19 (br. s, 12H), 1.40–1.60 (m, 4H), 2.20–2.38 (m, 4H)	−1.73 (Me ₃ Si), 14.08 (C ₁₃), 16.52 (C ₁), 22.63, 23.68, 23.88, 27.71, 29.13, 29.26, 29.37, 31.81 (C ₂ , C ₃ , C ₇ –C ₁₂), 42.56 (C ₄ or C ₆), 42.81 (C ₆ or C ₄), 211.84 (C ₅)
4c	1715 (vs), 1255 (m), 860 (vs), 840 (vs), 740 (w)	−0.10 (s, 9H), 0.35–0.48 (m, 2H), 1.10–1.33 (m, 6H), 1.40–1.60 (m, 2H), 2.07 (s, 3H), 2.36 (t, 2H, <i>J</i> = 7.4)	−1.71 (Me ₃ Si), 16.57 (C ₁), 23.69, 23.76, 28.84, 29.80, 33.27 (C ₂ –C ₅ , C ₈), 43.80 (C ₆), 209.39 (C ₇)
4d	1700 (vs), 1250 (m), 860 (vs), 840 (vs), 740 (w)	−0.07 (s, 9H), 0.38–0.52 (m, 2H), 0.81–0.92 (m, 3H), 1.24 (br. s, 14H), 1.45–1.65 (m, 4H), 2.36 (t, 4H, <i>J</i> = 7.4)	−1.69 (Me ₃ Si), 14.05 (C ₁₄), 16.61 (C ₁), 22.58, 23.73, 23.81, 23.84, 28.96, 29.06, 29.20, 31.66, 33.34 (C ₂ –C ₅ , C ₉ –C ₁₃), 42.79 (C ₆ , C ₈), 211.85 (C ₇)
5a	1730 (vs), 1715 (vs)	1.46–1.55 (m, 4H), 1.75–1.92 (m, 2H), 2.09 (s, 3H), 2.29 (t, 2H, <i>J</i> = 7.2), 2.33–2.48 (m, 6H), 3.62 (s, 3H)	18.80, 23.11, 23.17 (C ₅ , C ₇ , C ₈), 29.90, 32.99, 41.47, 42.46, 43.39 (C ₂ , C ₄ , C ₆ , C ₉ , C ₁₁), 51.56 (MeO), 173.62 (C ₁), 208.75 (C ₅ or C ₁₀), 209.83 (C ₁₀ or C ₅)
5b	1710 (vs), 1680 (vs)	0.80–0.94 (m, 3H), 1.25 (br. s, 8H), 1.46–1.82 (m, 6H), 2.38 (t, 2H, <i>J</i> = 7.4), 2.45 (t, 2H, <i>J</i> = 6.5), 2.97 (t, 2H, <i>J</i> = 6.9), 7.38–7.65 (m, 3H _{arom}), 7.88–8.05 (m, 2H _{arom})	14.04 (C ₁₃), 22.57, 23.39, 23.71, 23.82, 29.04, 29.17, 31.63 (C ₃ , C ₄ , C ₈ –C ₁₂), 38.30 (C ₂), 42.51 (C ₅ or C ₇), 42.85 (C ₇ or C ₅), 127.97, 128.54, 132.95, 136.86 (Ph), 199.98 (C ₁), 211.16 (C ₆)
5c	1710 (vs)	0.88 (t, 3H, <i>J</i> = 7.4), 1.14–1.30 (m, 4H), 1.42–1.68 (m, 6H), 2.25–2.50 (m, 6H), 3.65 (s, 2H), 7.15–7.35 (m, 5H _{arom})	13.74 (C ₁₂), 17.25, 23.44, 23.52, 28.79, 28.90 (C ₄ –C ₇ , C ₁₁), 41.78, 42.60, 44.67 (C ₃ , C ₈ , C ₁₀), 50.13 (C ₁), 126.92, 128.65, 129.34, 134.28 (Ph), 208.46 (C ₂ or C ₉), 211.39 (C ₉ or C ₂)
5d	1710 (vs), 1690 (vs)	0.75–1.02 (m, 3H), 1.05–1.80 (m, 18H), 2.25–2.50 (m, 4H), 2.94 (t, 2H, <i>J</i> = 7.2), 7.20–7.60 (m, 3H _{arom}), 7.88–8.05 (m, 2H _{arom})	14.03 (C ₁₅), 22.56, 23.63, 23.70, 23.84, 24.09, 29.04, 29.18, 29.25, 31.63 (C ₃ –C ₆ , C ₁₀ –C ₁₄), 38.43 (C ₂), 42.62 (C ₇ or C ₉), 42.81 (C ₉ or C ₇), 127.99, 128.51, 132.86, 136.97 (Ph), 200.41 (C ₁), 211.59 (C ₈)

^a Recorded on a Perkin–Elmer 381 spectrometer in CHCl_3 as solvent. ^b Recorded on a Varian XL 200 spectrometer. ¹H NMR data were measured at 200 MHz and ¹³C data at 50.3 MHz.

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