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Silylketenes under Kulinkovich conditions: alkene/ketene exchange versus nucleophilic addition. Application to the stereoselective preparation of vinylcyclopropanols

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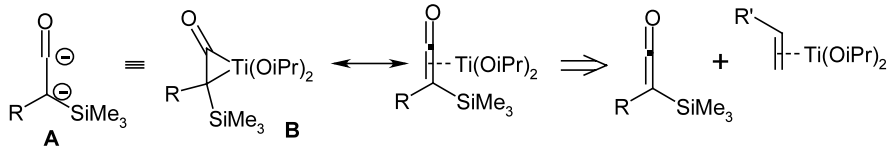
Abstract—Silylketenes react under Kulinkovich conditions through two competitive pathways: alkene/ketene exchange versus nucleophilic addition. In both cases, the organotitanium intermediate reacts with an aldehyde to yield an adduct which can undergo an elimination to yield a vinylcyclopropanol or an α,β-unsaturated carbonyl compound.

Silylketenes occupy a special place among ketenes because of both their stability and their ambident reactivity.[1] Indeed these molecules, discovered by Shchukovskaya in 1965,[2] can be isolated and stored for several months at −30°C. Moreover, along with classic electrophilic character, silylketenes can on some occasions display a nucleophilic behaviour. This is the case when they are paired with aldehydes in the presence of Lewis acids to form β-lactones, a reaction first reported by Zaisteva and Baukov in 1975.[3] As part of our long-running interest in these ketenes,[4] we wondered if it would be possible to transform them into bis-nucleophiles, such as ketene 1,2-dianion **A** (Scheme 1).

The low-valent titanium chemistry discovered by Kulinkovich in 1989[5] led us to propose titanacyclopropanone **B**, which could result from an alkene/ketene exchange on the titanium(II) complex, as a potential synthetic equivalent of ketene dianion **A**. Indeed, alkene/alkene and alkene/alkyne exchanges represent a very important development of the Kulinkovich reaction. They have been studied in detail by several authors[6] and have been discussed in detail in several recent reviews dedicated to this reaction.[7] A recent communication[8] reporting on the formation of vinylcyclopropanols (1-ethenylcyclopropanols) through Kulinkovich cyclopropanation and Peterson olefination prompted us to report our preliminary results on the reactivity of silylketenes towards these low-valent titanium reagents.

The study was carried on decyltrimethylsilylketene **1**, which was prepared in 67% yield over two steps from ethoxyacetylene,[4d] and with titanium(II) reactants prepared from *c*-HexMgCl or *i*-PrMgCl and Ti(O*i*-Pr)$_4$. In the absence of an electrophile and with *c*-HexMgCl (Table 1, entry 1), we only recovered a large proportion of ketene **1**. When acetaldehyde was added to the reaction mixture (Table 1, entry 2), hydroxyenone **2** and α,β-unsaturated aldehyde **3** were both obtained as single diastereomers along with some starting silylketene **1** (Scheme 2).[9]



Scheme 1.

Keywords: silylketene; low-valent titanium; exchange; aldehyde.
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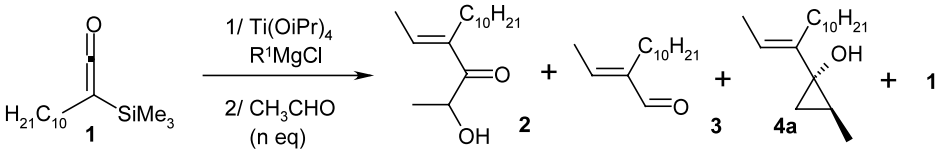
Table 1. Reaction between silylketene **1** and $Ti(Oi\text{-}Pr)_4/R^1MgCl$ in the presence (or not) of acetaldehyde

	R^1	*n*	**2** (%)	**3** (%)	**4a** (%)	**1** (recovered) (%)
1	*c*-Hex	0	–	–	–	61
2	*c*-Hex	2	33	6	–	18
3	*i*-Pr	4	26	–	26	12



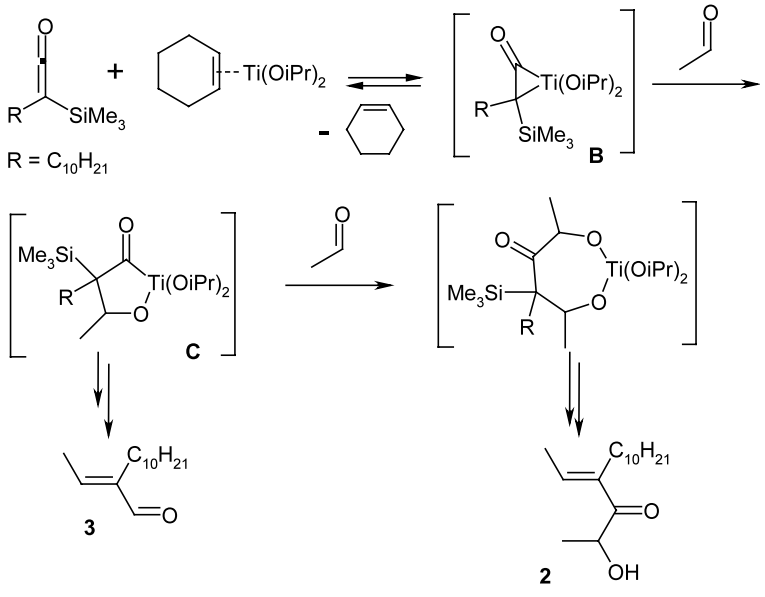
Scheme 2.

The formation of hydroxyenone **2** and aldehyde **3** can be accounted for through a single mechanism involving the expected alkene/ketene exchange as the initial step (Scheme 3). Aldehyde **3** results from a monocondensation, of the so-formed titanacyclopropanone **B** with acetaldehyde, followed by a stereoselective elimination[10] while the stereoselective formation of hydroxyenone **2** implies a second condensation of oxatitanacyclopentanone **C** with acetaldehyde, again completed by a similar elimination.[10]

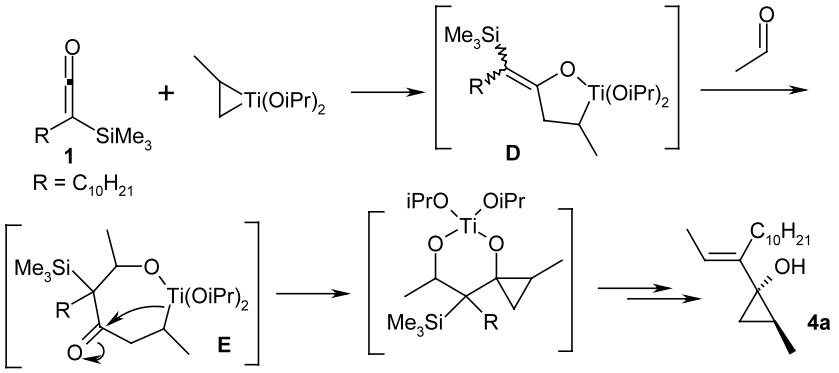
When using *i*-PrMgCl to reduce the Ti(IV) reagent (Table 1, entry 3), we also observed the concomitant formation of a single diastereomer of vinylcyclopropanol **4a**. Its formation probably results from a completely different mechanism which competes with the exchange mechanism. Silylketene **1** now undergoes nucleophilic addition with the titanacyclopropane reagent to form titanium enolate **D** which then condenses with acetaldehyde. The resulting intermediate **E** then undergoes cyclopropanation and elimination[10] to yield the vinylcyclopropanol (Scheme 4). The competition between the two mechanisms does not occur when *c*-HexMgCl is involved; this observation is in agreement with the literature since the resulting Ti(II) reagent is known to favour exchange processes.[6c]

As vinylcyclopropanols are valuable synthetic intermediates which are not easy to prepare, we have examined the influence of various parameters on the yield of the reaction as well as its scope (Scheme 5). Vinylcyclopropanols **4a–e** were obtained from aliphatic (Table 2, entries 1,[11] 6 and 8) as well as aromatic aldehydes (entries 9 and 10). Diethyl ether was far better than THF as the solvent (compare entries 1–3 and 4). $ClTi(Oi\text{-}Pr)_3$ is as efficient as $Ti(Oi\text{-}Pr)_4$ (entries 6 and 7) while Cp_2TiCl_2 is clearly not a good titanium source for this reaction (entries 1 and 5). Finally, a large excess of reagent does not improve the yield of the reaction (entry 3).

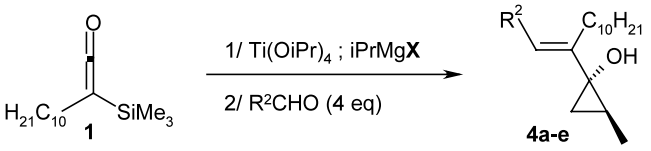
In summary, we have established that an alkene/ketene exchange is possible and leads to the formation of a synthetic equivalent of a ketene dianion which behaves



Scheme 3.



Scheme 4.



Scheme 5.

as a bis-nucleophile to produce hydroxyenones stereoselectively. Moreover, depending on the Ti(II) reagent involved, it is also possible to prepare, from a silylketene and various aldehydes, vinylcyclopropanols with complete stereoselectivity. Although yields are moderate, both types of products result from a one-pot sequential formation of two or three C–C bonds followed by an elimination. Studies are currently underway to examine the scope of these reactions, to study the mechanisms involved, particularly that of the elimination,[10] and to try to improve their yields.

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Table 2. Vinylcyclopropanols **4a–e** from silylketene **1** and various aldehydes

	Ti(O*i*-Pr)$_4$ (equiv.)	X (equiv.)	Solvent	*T* (°C)	R^2	**4a–e** (%)
1	1.25	Cl (2.75)	Et_2O	−30	-C_5H_{11}	**4b**: 42
2	1.25	Br (2.75)	Et_2O	−40	-C_5H_{11}	**4b**: 36
3	2.5	Cl (5.5)	Et_2O	−30	-C_5H_{11}	**4b**: 41
4	1.25	Cl (2.75)	THF	−20	-C_5H_{11}	**4b**: <10
5	Cp_2TiCl_2:1.25	Cl (2.75)	Et_2O	−30	-C_5H_{11}	**4b**: 13
6	ClTi(O*i*-Pr)$_3$:1.25	Cl (2.75)	Et_2O	−30	-CH_3	**4a**: 34
7	1.25	Cl (2.75)	Et_2O	−30	-CH_3	**4a**: 33
8	1.25	Cl (2.75)	Et_2O	−30	-C_2H_5	**4c**: 33
9	1.25	Cl (2.75)	Et_2O	−30	-C_6H_5	**4d**: 25
10	1.25	Cl (2.75)	Et_2O	−30	-2-Furyl	**4e**: 31

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9. Typical procedure for the preparation of hydroxyenone **2**: *c*-HexMgCl (1.6 mmol, 0.8 mL of a 2 M solution in Et_2O) was added under argon to a cooled (−30°C) solution of Ti(O*i*-Pr)$_4$ (0.68 mmol, 0.2 mL) in Et_2O (1.3 mL). A solution of decyl(trimethylsilyl)ketene **1** (0.53 mmol, 138 mg) in Et_2O (0.8 mL) was then added and the solution allowed to warm up to −10°C. After 4 h at that temperature, acetaldehyde (3.6 mmol, 0.2 mL) was added and stirring was continued for an additional 3 h. Finally, the reaction was quenched with cold water (1 mL) and the resulting suspension filtered through Celite. After the solvents were removed in vacuo, flash chromatography (petrol/ether: 95/5) of the crude product led to α,β-unsaturated aldehyde **3** (6 mg, 6%) and hydroxyenone **2** (45 mg, 33%) along with recovered starting ketene **1** (18%). **2**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.60 (1H, q, $J=7.0$ Hz), 4.85 (1H, quint., $J=6.7$ Hz), 3.71 (1H, d, $J=6.0$ Hz), 2.38 (1H, $\frac{1}{2}$ AB, m, $J_{AB}=13.8$ Hz), 2.24 (1H, $\frac{1}{2}$ AB, m, $J_{AB}=13.8$ Hz), 1.89 (3H, d, $J=7.0$ Hz), 1.41–1.11 (16H, m), 1.30 (3H, d, $J=7.0$ Hz), 0.85 (3H, t, $J=7.1$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.4 (s), 140.0 (s), 139.4 (d), 68.3 (d), 32.0 (t), 29.7 (t), 29.5 (3C) (t), 29.4 (t), 28.2 (t), 25.8 (t), 22.7 (t), 23.0 (q), 14.8 (q), 14.2 (q). IR (film): 3380, 2924, 2843, 1666, 1091 cm^{-1}. LRMS for $C_{16}H_{30}O_2$: $[M+H]^+$: 255; MS/MS (30 eV): 255, 237, 219, 109, 95, 57.
10. These reactions formally eliminate Me_3SiOH and hence can be viewed as a Peterson olefination reaction. However, further studies on these reactions are necessary for a better understanding of their mechanism.
11. Typical procedure for the preparation of vinylcyclopropanol **4b**: Ti(O*i*-Pr)$_4$ (1 mmol, 0.3 mL) was added at room temperature under argon to a solution of decyl(trimethylsilyl)ketene **1** (0.8 mmol, 203 mg) in Et_2O (0.8 mL). The solution was then cooled to −78°C before *i*-PrMgCl (2.2 mmol, 1.1 mL of a 2.2 M solution in Et_2O) was added dropwise. The reaction mixture was then allowed to warm up to −35°C and after 2 h stirring at that temperature, hexanal (1.5 mmol, 0.18 mL) was added. After 5 h at the same temperature the reaction was quenched with water (1 mL). Filtration through Celite and removal of the solvents in vacuo led to the crude product which was purified by flash chromatography on silica (petrol/ether: 9/1) to yield vinylcyclopropanol **4b** (120 mg) in 42% yield. **4b**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.32 (1H, t, $J=7.3$ Hz), 2.22 (1H, ddd, $J=13.4$, 10.6, 5.6 Hz), 2.06 (1H, ddd, $J=13.4$, 10.6, 5.8 Hz), 2.01 (2H, q, $J=7.3$ Hz), 1.52–1.38 (2H, m), 1.36–1.20 (20H, m), 1.20 (1H, qd, $J=9.8$, 6.3 Hz), 0.86 (3H, t, $J=6.9$ Hz), 0.85 (3H, t, $J=6.9$ Hz), 0.82 (3H, t, $J=6.3$ Hz), 0.76 (1H, dd, $J=9.9$, 5.2 Hz), 0.47 (1H, t, $J=5.8$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.8 (s), 129.2 (d), 64.7 (s), 32.0 (t), 31.7 (t), 30.5 (t), 29.9 (t), 29.8 (t), 29.7 (2C) (t), 29.6 (t), 29.4 (t), 29.2 (t), 27.7 (t), 22.8 (t), 22.6 (t), 20.9 (d), 18.5 (t), 14.6 (q), 14.2 (q), 13.3 (q). IR (film): 3376, 2924, 2855, 1663, 1460, 1375, 1190 cm^{-1}. LRMS for $C_{21}H_{40}O$: $[M+NH_4]^+$: 326; MS/MS (20 eV): 326 $[(M+NH_4)^+]$, 309 $[(M+H)^+]$, 291, 221, 165, 151, 123, 109, 95, 81, 71, 57.