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# A new route to silyl-substituted cyclobutenones and silylketenes

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## ARTICLE INFO

# ABSTRACT

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## 1. Introduction

1-Alkenyl(silyl)ketenes ('silyl(vinyl)ketenes') **1**<sup>1</sup> show remarkable stability, but are sufficiently reactive especially in cycloaddition chemistry to make them attractive synthetic buildingblocks,<sup>2-4</sup> including in applications such as natural product synthesis.<sup>5</sup> Four main routes have been described for their synthesis which, however, suffers from certain drawbacks (Scheme 1). Thus, the dehydrohalogenation of appropriately substituted acyl chlorides **2** is limited to produce vinylketenes in which  $R^2 = H$  in order to avoid regiochemical ambiguity.<sup>6</sup> Similarly, the Wolff rearrangement of  $\alpha$ , $\beta$ -unsaturated  $\alpha'$ -diazoketones **3** works best for purely aliphatic 1-alkenyl substitution.<sup>2</sup> The outcome of the reaction of silvl-substituted alkynes **4** with Fischer carbene complexes **5** depends on the size of the silvl substituent and is limited to the preparation of vinylketenes in which R<sup>4</sup> is an alkoxy group.<sup>5,7,8</sup> Finally, the [2 + 2] cycloaddition of aryl(silyl)acetylenes **4** ( $R^2$  = aryl) with dichloroketene and the subsequent dehalogenation give 2-silyl-cyclobutenones and from there the corresponding silylketenes, but the regioselectivity in the cycloaddition step can only be secured when  $R^2$  is an aryl substituent.<sup>2</sup> So it appeared attractive to develop an independent method for regiospecific introduction of a silyl substituent into the cyclobutenone ring.

# 2. Results and discussion

Dialkyl squarates **7** are excellent starting materials for the synthesis of cyclobutene(di)ones.<sup>9,10</sup> In a convenient one-pot reaction



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Scheme 1. Routes to silyl(vinyl)ketenes.

sequence, carbanions are first added to **7**, the resulting alkoxide is trifluoroacetylated to **8**, and then a nucleophile is introduced in an  $S_N2'$  process to give intermediate **9** (Scheme 2).<sup>11–13</sup> Thus, with water as nucleophile cyclobutenediones are formed via the hemiacetal, the use of alcohols as nucleophile leads to acetals, and the addition of amines produces cyclobutenimines.<sup>14</sup> We reasoned that this approach might be amenable to the introduction of a silyl residue if a silyl anion<sup>15</sup> is used as attacking nucleophile in the 1,2



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**Scheme 2.** Introduction of a substituent  $R^2$  into a squarate.

addition step ( $\mathbb{R}^2$  = silyl). In fact, silyl anions **10a**–**c** turned out to give a smooth addition to squarate **7** ( $\mathbb{R}^1$  = Me) and, depending on the method of work-up, provide diones of type **7** (one silyl instead of MeO) or acetals **11a**–**c** (Scheme 3).<sup>16</sup> Isolated yields are good for **11a** and **11b**, but probably due to steric reasons, **11c** is formed only in trace amounts (Table 1). Products **11** are stable at room temperature and show no apparent tendency to undergo ring opening to silylketenes **12**.

Interestingly, the remaining methoxy group in methoxycyclobutenone **11a** can be exchanged for a methyl or phenyl group following the addition/substitution approach outlined in Scheme 2. Thus, with methyl or phenyllithium and after aqueous work-up, cyclobutenones **13a** (57%) and **13b** (77%) are formed (Scheme 4).

In a further modification, the acetal group in acetals **11a**,**b** and **13a,b** can be transformed into a thioacetal group which, if a dithiolane is formed, can be considered as a latent thione unit (Scheme 5).<sup>17</sup> As in earlier studies,<sup>18,19</sup> zirconium tetrachloride turned out to be the most efficient Lewis acid catalyst for this transformation. However, yields remain relatively low as in contrast to acetals 11 and 13, thioacetals 14 show, even at room temperature, a pronounced tendency to undergo electrocyclic ring opening to give silvlketenes 15 which display variable stability. Thus, immediately after chromatographic purification, products 14 already show the characteristic ketene vibration at 2100 cm<sup>-1</sup> in the IR spectra. The best yield is obtained for thioacetal 14c, followed by 14d, while the methoxy-substituted derivative 14a is isolated in lower yield and 14b only in trace amounts (Table 1). For 14c, complete conversion into silylketene **15b**<sup>20</sup> is achieved by heating to 90 °C in toluene for 30 min. However, due to the limited stability of ketenes 15 and the corresponding species derived from acetals 13 it is advantageous to use precursors 12-14 in reactions and generate the silylketene in situ.



Scheme 3. Synthesis of silyl-substituted cyclobutenones (for yields see Table 1).

Starting materials, products, and yields in the reactions of Schemes 3 and 5

Table 1

Entry	Starting material	Product	Yield (%)
1	<b>7</b> (R <sup>1</sup> = Me)	11a	82
2	<b>7</b> (R <sup>1</sup> = Me)	11b	49
3	<b>7</b> (R <sup>1</sup> = Me)	11c	Trace
6	11a	14a	29
7	11b	14b	Trace
8	13a	14c	57
9	13b	14d	32



**13b**:  $R^3 = Ph (77\%)$ 

Scheme 4. Methoxy substitution in methoxy-cyclobutenone 11a.



Scheme 5. Formation of thioacetals 14 and electrocyclic ring opening to ketenes 15 (for yields see Table 1).

In previous studies, silylketenes have been shown to be useful substrates for reaction with C<sub>1</sub> transfer reagents to give cyclopentenones in a [4+1] approach.<sup>21-23</sup> A particularly smooth reaction had been observed for (trimethylsilyl)diazomethane<sup>21</sup> and this is now confirmed for the reaction with the novel silylcyclobutenones/silylketenes **11–14/15** (Scheme 6).<sup>24</sup> Generally good yields  $(50–74\%)^{25}$  are obtained both from acetals **11** and **13** and from thioacetals **14** implying that at temperatures above 90 °C ketene intermediates of type **15** are also formed from acetals **11** and **13** which at room temperature are stable compounds with no apparent tendency to undergo electrocyclic ring opening. However, only trace amounts of cyclopentenone products **16c**,**f** are formed from silylcyclobutenones **13a** and **14b** where the corresponding ketene intermediates **15** are apparently quite labile and preferably undergo decomposition.

The inherent  $4\pi$  system in vinylketenes **15** invites the use of precursors **11**, **13**, and **14** as dienes in Diels–Alder chemistry.<sup>2</sup> Here



11a,b, 13a,b, 14a-d

**16a**:  $R^1 = R^2 = Me$ ,  $R^3 = X = OMe (51\%)$  **b**:  $R^1 = Me$ ,  $R^2 = Ph$ ,  $R^3 = X = OMe (54\%)$  **c**:  $R^1 = R^2 = R^3 = Me$ , X = OMe (trace) **d**:  $R^1 = R^2 = Me$ ,  $R^3 = Ph$ , X = OMe (77%) **e**:  $R^1 = R^2 = Me$ ,  $R^3 = OMe$ ,  $X = SCH_2 (74\%)$  **f**:  $R^1 = Me$ ,  $R^2 = Ph$ ,  $R^3 = OMe$ ,  $X = SCH_2 (trace)$  **g**:  $R^1 = R^2 = R^3 = Me$ ,  $X = SCH_2 (74\%)$ **h**:  $R^1 = R^2 = Me$ ,  $R^3 = Ph$ ,  $X = SCH_2 (50\%)$ 



Scheme 7. Formal Diels-Alder reactions of silylketene precursors 14. Reagents and conditions: (a) TCNE, toluene, 110 °C, 12 h (for 14c,d); (b) N-methyl-4-nitrobenzaldimine, toluene, 110 °C, 24 h (for 14d); (c) TMS-N=CH-Ph or TMS-N=CH-CH=CH-Ph, cat. Zn(Otf)<sub>2</sub>, THF, rt, 24 h (for 14c,d); aq work-up.

we had little success with olefinic reaction partners. Only tetracyanoethylene gives a smooth reaction with thioacetals **14c,d**, but no cycloadduct 17 with 3-methoxy-cyclobutenone 14a (Scheme 7). The alternative 2-alkenyl-cyclobutanone structure for 17 can be ruled out because of a carbonyl vibration at relatively low wavenumber around 1700 cm<sup>-1</sup>.

[2 + 2] Cycloadditions of cyclobutenones **14** with C=N systems turned out to be more successful. In particular, **14d** undergoes a smooth reaction with *N*-methyl-4-nitrobenzaldimine to give β-lactam **18** in two diasteromeric forms with a characteristic carbonyl absorption at 1740 cm<sup>-1</sup> (Scheme 7). Under the reaction conditions, ketene **15a** from cyclobutenone **14a** apparently decomposes and 14c/15c gives no reaction. In contrast, N-silyl-imines and silylketene precursors **14c,d** give  $\delta$ -lactams **19a–d**,<sup>26</sup> but to obtain the indicated yields of 16-72% catalysis by zinc triflate is required; the aqueous work-up leads to N-desilylation.

## 3. Conclusion

The addition/substitution method (Scheme 2) offers convenient access to silvlcyclobutenones. Acetals 11 show no spontaneous electrocyclic ring opening to silvlketenes 12, but the ketene species is apparently formed on heating with silvldiazomethane and trapped to give cyclopentenones 16a-d. Thioacetals 14a-d are in equilibrium with silvlketenes 15, which can be trapped to 16-19, but decomposition of 15 sometimes interferes.

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- Cyclobutenone **11a**, Typical Procedure: Me<sub>2</sub>PhSiLi (70 mL, 0.5 M in THF, 35.0 mmol) was added dropwise to **7** ( $\mathbb{R}^1$  = Me; 4.886 g, 34.4 mmol) in dry 16. THF (500 mL) at -78 °C. After 20 min, TFAA (5.5 mL, 34.4 mmol) was added and after another 20 min dry MeOH (40 mL). The mixture was allowed to warm to rt over 30 min with stirring and aq NaHCO3 (20%, 250 mL) added. The product was extracted with ether (2  $\times$  250 mL), the ethereal solution washed with brine (2  $\times$  150 mL), dried (MgSO4) and concentrated in vacuo. Purification by flash chromatography (SiO<sub>2</sub>, petroleum ether/EtOAc = 101) yielded cyclobutenone **11a** (8.212 g, 46%). Yellow oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.56 (m, 2H), 7.38 (m, 3H), 3.95 (s, 3H), 3.53 (s, 6H), 0.42 (s, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 193.5, 192.1, 136.9, 133.7, 131.5, 129.5, 128.0, 115.0, 60.2, 53.5, -2.5 ppm. IR (film): v = 1750 cm<sup>-1</sup>. HRMS (ESI): [M+Na]<sup>+</sup> found 315.1023, calcd 315.1023.
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- Selected data of compounds: Ketene 15b: slightly yellow liquid. <sup>1</sup>H NMR 20. (400 MHz, CDCl<sub>3</sub> = 7.26):  $\delta$  = 7.60 (m, 2H), 7.39 (m, 1H), 7.29–7.17 (m, 3H), 3.38 (m, 4H, SCH<sub>2</sub>), 1.77 (s, 3H), 0.49 (s, 6H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub> = 77.4):  $\delta$  = 198.6, 137.1, 133.8, 129.6, 85.3, 38.8, 38.1, 24.8, 0.9, -1.6. IR (film): v = 2958, 2086, 1589, 1428, 1252, 1115, 982, 813, 734, 701 cm<sup>-1</sup>. HRMS (EI): [M]<sup>+</sup> found 306.0569, calcd 306.0568.
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- 25. Cyclopentenone 16a: waxy solid, mp 74 °C. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub> = 7.26):  $\delta$  = 7.37 (m, 1H), 7.21 (m, 4H), 3.47 (s, 3H), 3.28 (s, 3H), 3.14 (s, 3H), 2.41 (s, 1H), 0.06 (s, 3H), 0.04 (s, 3H), 0.00 (s, 9H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub> = 77.4):  $\delta = 206.7, 188.8, 140.6, 134.5, 130.0, 128.9, 116.0, 107.9, 62.4, 52.4, 52.3, 51.1,$ 0.1, 0.0. IR (film): v = 2950, 2899, 2834, 1678, 1619, 1458, 1428, 1308, 1246, 1147, 1110, 1045, 970, 841, 816, 777, 734, 701, 650 cm<sup>-1</sup>. HRMS (TOF-MS ES): [M+Na]<sup>+</sup> found 401.1591, calcd 401.1584.
- 26  $\delta$ -Lactam **19c**: colorless crystals, mp 205 °C. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub> = 7.26): δ = 7.91 (m, 2H), 7.56 (m, 2H), 7.24 (m, 11H), 6.42 (br s, 1H), 5.29 (s, 1H), 2.97 (m, 4H), 0.45 (s, 3H), 0.16 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub> = 77.4):  $\delta$  = 177.4, 139.3, 137.0, 136.9, 133.0, 130.5, 129.5, 129.7, 129.5, 128.9, 128.5, 67.7, 48.2, 39.2, 38.4, 1.5, 0.0. IR (KBr): v = 3166, 3056, 1676, 1491, 1445, 1427, 1374, 1348, 1303, 1246, 1111, 1018, 835, 818, 775, 730, 701, 652, 610, 544 cm<sup>-1</sup>. HRMS (TOF-MS ES): [M+Na]<sup>+</sup> found 496.1207, calcd 496.1201.