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Tetrahedron Letters 47 (2006) 1797–1800

Tetrahedron Letters

GaCl$_3$ Promoted one-step α,α-diethynylation and α,α-diethenylation reactions of silyl enol ethers

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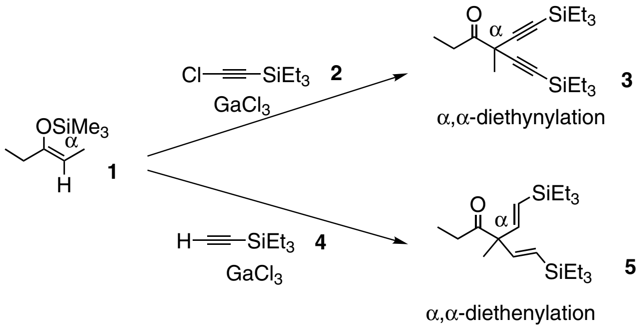
Received 12 December 2005; revised 5 January 2006; accepted 6 January 2006
Available online 26 January 2006

Abstract—In the presence of GaCl$_3$ and 2,6-di(*tert*-butyl)-4-methylpyridine, α-monosubstituted silyl enol ethers were α,α-diethynylated with a chlorosilylacetylene in one step. An analogous reaction using a silylacetylene gave α,α-diethenylated ketones.

Dialkylation at the carbonyl α-position is a useful method to construct quaternary carbon centers.[1,2] One-step α,α-diethynylation and α,α-diethenylation, however, were not known, although such compounds with highly functionalized quaternary carbons could have various potential uses in organic synthesis. Several stepwise methods were reported: An α,α-diethynylated α-hydroxy ketone was prepared from an α,α-dimethoxyalkanoate and lithium acetylide followed by deacetalization;[3] α,α-diethenyl propanoates were obtained by the pyrolysis of 5-methylbicyclo[2.1.0]pentanecarboxylates;[4] α,α-bis(β-hydroxyethyl)phenylacetonitrile was converted to α,α-diethenylphenylacetic acid by elimination;[5] α,α-diethenylated thioesters were synthesized by the sequential ethenylation of silyl enol ethers.[6]

Previously, we reported GaCl$_3$ catalyzed α-ethynylation reaction of α,α-disubstituted silyl enol ethers with chlorotriethylsilylacetylene **2**.[7] This catalytic α-ethynylation, however, did not proceed with α-monosubstituted silyl enol ethers. Described here is the finding that one-step α,α-diethynylation of such silyl enol ethers takes place under appropriate conditions (Scheme 1). The α,α-diethenylation of silyl enol ethers with triethylsilylacetylene **4** is also described.



Scheme 1.

As described previously,[7] the reaction of 6-trimethylsiloxy-5-undecene **1a** (cis:trans = 1:2) and **2** (6 equiv) in the presence of a catalytic or a stoichiometric amount of GaCl$_3$ in methylcyclohexane at 130 °C gave very small amounts of the ethynylated product, if any. The addition of 2,6-di(*tert*-butyl)-4-methylpyridine (1.0 equiv),[8] however, gave a considerable amount of α,α-diethynylated ketone. Under an argon atmosphere, a mixture of **1a**, **2** (6 equiv), and GaCl$_3$ (1.0 equiv) in chlorobenzene was heated at 150 °C for 5 h, and 5,5-bis(triethylsilylethynyl)-6-undecanone **3a** was obtained in 48% yield.[9] The diethynylation proceeded at the same α-carbon, and the gallium enolates involved in this reaction should be generated in two different modes: (1) transmetalation of silyl enol ether **1a** and GaCl$_3$; (2) deprotonation of the ethynylated ketone **6a** with GaCl$_3$ (Scheme 2).[8]

The reaction could be applied to several silyl enol ethers derived from acyclic and cyclic ketones, and α,α-diethynylated ketones **3a**–**i** were obtained in modest yields (Table 1). The reactivity of silyl enol ethers derived from cyclic ketones was influenced by the ring size (entries 8–10). While large membered ring compounds **1i** and

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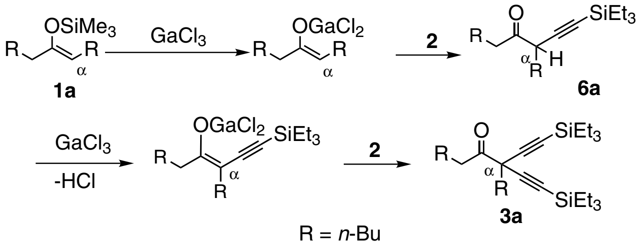
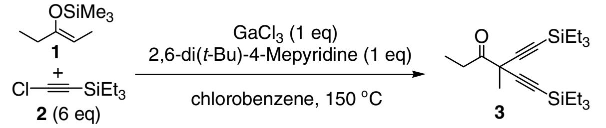
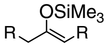
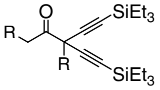
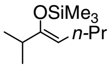
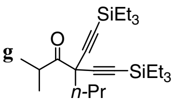
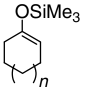
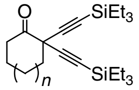
doi:10.1016/j.tetlet.2006.01.025



Scheme 2.

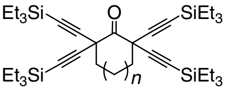
Table 1. α,α-Diethynylation reaction of silyl enol ether



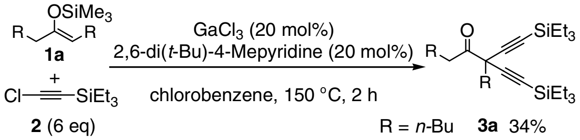
Entry	Substrate	Product	Time/h	Yield/%
				
1	R = n-Bu	**a**	5	48
2	R = Me	**b**	5	25
3	R = Et	**c**	5	42
4	R = n-C_9H_{19}	**d**	5	36
5	R = i-Pr	**e**	5	35
6	R = Ph	**f**	5	23
7		**g** 	5	42
				
8	$n = 1$	**h**	1.5	6
9	$n = 7$	**i**	12	32[a]
10	$n = 10$	**j**	5	30[b]

[a] **7i** was obtained in 6% yield.

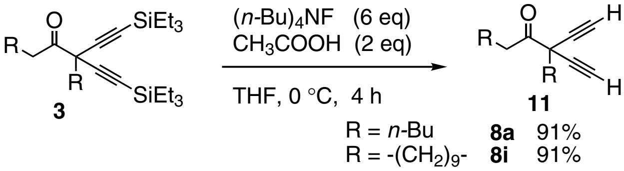
[b] **7j** was obtained in 3% yield.



7i $n = 7$
7j $n = 10$



Scheme 3.



Scheme 4.

1j gave α,α-diethynylated ketones **3i** and **3j** in acceptable yields (entries 9 and 10), the reaction of 2-trimethylsiloxy-1-cyclohexene **1h** gave **3h** only in 6% yield (entry 8). Notably, small amounts of α,α,α′,α′-tetraethynylated ketones **7i** and **7j** were obtained in the former reactions.

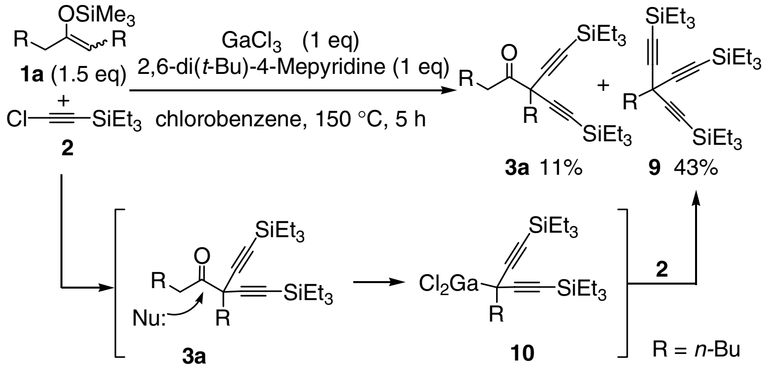
Since $GaCl_3$ was regenerated by the β-elimination, the α,α-diethynylation reaction can in principle be catalytic. A mixture of **1a** and **2** (6 equiv) in chlorobenzene was heated at 150 °C with $GaCl_3$ (20 mol %) and 2,6-di(*tert*-butyl)-4-methylpyridine (20 mol %) for 2 h giving **3a** in 34% yield (Scheme 3). It could be calculated that 1 mol of $GaCl_3$ was used for 3.4 times of the C–C bond formation.

The products could be desilylated giving the parent α,α-diethynyl ketones. When **3a** and **3i** were treated with tetrabutylammonium fluoride (6 equiv) and acetic acid (2 equiv) in THF at 0 °C for 4 h, **8a** and **8i** were obtained both in 91% yields (Scheme 4).

It was noted that C–C bond cleavage occurred in the presence of an excess silyl enol ether. When **1a** (1.5 equiv) and **2** were reacted with $GaCl_3$ (1 equiv) and 2,6-di(*tert*-butyl)-4-methylpyridine (1 equiv) at 150 °C for 5 h, **3a** was obtained in 11% (based on **2**), which was accompanied by 1-triethylsilyl-3,3-di(triethylsilylethynyl)-1-heptyne **9** in 43% yield (based on **2**). The product **9** should be formed via deacylation of **3a** by nucleophiles such as silyl enol ether or chloride, which was followed by the ethynylation of the organogallium intermediate **10** (Scheme 5).[10]

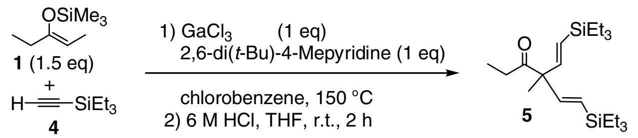
The above results suggested that α,α-ethenylation could also proceed using $GaCl_3$ by reacting silyl enol ethers with a silylated acetylene.[6] Silyl enol ether **1a** (1.5 equiv) and **4** were reacted with $GaCl_3$ (1 equiv) and 2,6-di(*tert*-butyl)-4-methylpyridine (1 equiv) in chlorobenzene at 150 °C for 45 min. Then the reaction was quenched with water, and the ^{1}H NMR analysis of the mixture showed the presence of α-(γ-gallio-γ-silylethenyl)-α-silylethenyl ketone **11a** in 41% yield, δ 6.09 (d, 1H, $J = 19$ Hz), 5.90 (d, 1H, $J = 19$ Hz), and 6.24 (s, 1H). When the mixture was treated with 6 M HCl in THF for 2 h, 5,5-bis(2-triethylsilylethenyl)-6-undecanone **5a** was obtained in 40% yield.[11] The α,α-diethenylation reaction could be applied to several silyl enol ethers (Table 2).

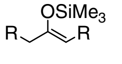
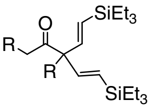
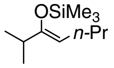
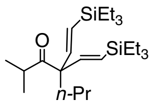
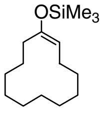
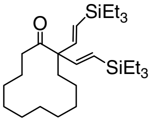
To summarize, α-monosubstituted silyl enol ethers reacted with a chlorosilylacetylene in the presence of $GaCl_3$ and 2,6-di(*tert*-butyl)-4-methylpyridine giving α,α-diethynylated ketones. When a silylated acetylene was reacted, α,α-diethenylated ketones were obtained. These reactions provide carbonyl compounds possessing highly functionalized quaternary α-carbon centers.



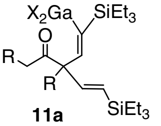
Scheme 5.

Table 2. α,α-Diethenylation of silyl enol ether



Entry	Substrate	Product	Time/min	Yield/%[a]
				
1	R = *n*-Bu	**a**	45	40
2	R = Et	**c**	45	37
3	R = *n*-C_9H_{19}	**d**	90	31
4	R = *i*-Pr	**e**	120	35
5		**g** 	120	40
6		**i** 	60	50

[a] Yield based on **4**.



11a R = *n*-Bu

Acknowledgement

The authors thank JSPS for financial supports.

References and notes

1. Reviews: House, H. O. In *Modern Synthetic Reactions*; Breslow, R., Ed.; W. A. Benjamin, INC: Menlo Park, CA, 1972, Chapter 9; Caine, D. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 3, Chapter 1.1. Mekelburger, H. B.; Wilcox, C. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, Chapter 1.4.
2. Millard, A. A.; Rathke, M. W. *J. Org. Chem.* **1978**, *43*, 1834; Dubois, J. E.; Saumtally, I.; Lion, C. *Bull. Soc. Chim. Fr.* **1982**, 318; Inoue, Y.; Toyofuku, M.; Taguchi, M.; Okada, S.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 885; Aranda, A.; Diaz, A.; Diez-Barra, E.; Hoz, A. de la; Moreno, A.; Sanchez-Verdu, P. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2427.
3. Omum, S. G. V.; Cook, J. M. *Tetrahedron Lett.* **1996**, *37*, 7185.
4. Jorgenson, M. J.; Clark, T. J. *J. Am. Chem. Soc.* **1968**, *90*, 2188.
5. Wilt, J. W.; Niinemae, R. *J. Org. Chem.* **1979**, *44*, 2533.
6. Arisawa, M.; Miyagawa, C.; Yoshimura, S.; Kido, Y.; Yamaguchi, M. *Chem. Lett.* **2001**, 1080; Also see: Yamaguchi, M.; Tsukagoshi, T.; Arisawa, M. *J. Am. Chem. Soc.* **1999**, *121*, 4074; Arisawa, M.; Akamatsu, K.; Yamaguchi, M. *Org. Lett.* **2001**, *3*, 789; Arisawa, M.; Miyagawa, C.; Yamaguchi, M. *Synthesis* **2002**, 138.
7. Amemiya, R.; Fujii, A.; Arisawa, M.; Yamaguchi, M. *J. Organomet. Chem.* **2003**, *686*, 94; Also see: Arisawa, M.; Amemiya, R.; Yamaguchi, M. *Org. Lett.* **2002**, *4*, 2209.
8. Amemiya, R.; Nishimura, Y.; Yamaguchi, M. *Synthesis* **2004**, 1307. We also developed an ethynylation reaction of ketones using a catalytic amount of trialkylgallium: Nishimura, Y.; Amemiya, R.; Yamaguchi, M. *Tetrahedron Lett.*, in press.
9. Under an argon atmosphere, a solution of $GaCl_3$ (1.0 M, 0.5 mmol) in methylcyclohexane (0.5 mL) was added dropwise to a mixture of **1a** (121 mg, 0.5 mmol), **2** (524 mg, 3.0 mmol), and 2,6-di(*tert*-butyl)-4-methylpyridine (103 mg, 0.5 mmol) in chlorobenzene (2 mL) at room temperature. The mixture was stirred for 5 h at 150 °C, and after being cooled to room temperature, water was added. The organic materials were extracted with ether. The combined organic layers were washed with 2 M HCl and brine, dried over $MgSO_4$, and concentrated. The residue was purified by flash column chromatography (hexane/ethyl acetate = 100/1) to give **3a** (107 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.58 (12H, q, $J = 8.0$ Hz), 0.89 (6H, q, $J = 7.2$ Hz), 0.98 (18H, t, $J = 8.0$ Hz), 1.25–1.41 (6H, m), 1.47–1.54 (2H, m), 1.62 (1H, quint, $J = 6.8$ Hz), 1.81–1.85 (2H, m), 2.91 (2H, t, $J = 7.2$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.5, 7.6, 14.1, 22.6, 22.7, 24.3, 27.5, 31.4, 37.2, 38.4, 49.4, 86.3, 104.2, 202.5. IR (neat) 2166, 1735, 727 cm^{-1}. MS (EI) *m*/*z* 446 (M^+, 57%), 87 ($M^+-C_{22}H_{39}Si_2$, 100%). HRMS Calcd for $C_{27}H_{50}OSi_2$: 446.3400. Found: 446.3399.

10. Amemiya, R.; Suwa, K.; Toriyama, J.; Nishimura, Y.; Yamaguchi, M. *J. Am. Chem. Soc.* **2005**, *127*, 8252.
11. Under an argon atmosphere, a solution of $GaCl_3$ (1.0 M, 1.0 mmol) in methylcyclohexane (1.0 mL) was added dropwise to a mixture of **1a** (363 mg, 1.5 mmol) and **4** (140 mg, 1.0 mmol) in chlorobenzene (2 mL) at room temperature. 2,6-Di(*tert*-butyl)-4-methylpyridine (205 mg, 1.0 mmol) was added, and stirring was continued for 45 min at 150 °C. After cooling to room temperature, THF (2 mL) and 6 M HCl (10 mL) were added, and the mixture was stirred for 2 h at room temperature. The organic materials were extracted with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by flash column chromatography (hexane/ethyl acetate = 100/1) to give **5a** (90 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.58 (12H, q, $J = 8.0$ Hz), 0.86 (6H, t, $J = 7.2$ Hz), 0.93 (18H, t, $J = 8.0$ Hz), 1.05–1.35 (6H, m), 1.49 (2H, quint, $J = 7.2$ Hz), 1.72–1.83 (2H, m), 2.37 (2H, t, $J = 7.2$ Hz), 5.67 (2H, d, $J = 19.2$ Hz), 6.19 (2H, d, $J = 19.2$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.4, 7.3, 13.8, 13.9, 22.5, 23.3, 24.1, 26.5, 31.5, 35.5, 39.1, 65.0, 128.3, 148.1, 210.4. IR (neat) 2954, 1710, 1604, 1458, 1415, 1377, 1237, 999, 787, 720 cm^{-1}. MS (EI) *m/z* 450 (M^+, 73%), 421 ($M^+{-}C_2H_5$, 9%), 379 ($M^+{-}C_5H_{11}$, 60%), 335 ($M^+{-}C_6H_{15}Si$, 50%), 115 ($M^+{-}335$, 100%). HRMS Calcd for $C_{27}H_{54}OSi_2$: 450.3713. Found: 450.3722.