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Oxovanadium-Induced Oxidative Desilylation for the Selective Synthesis of 1,4-Diketones

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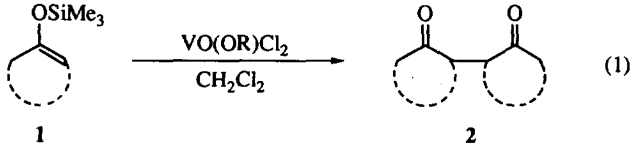
Abstract: Silyl enol ethers underwent the $VO(OR)Cl_2$-induced homo- or cross-coupling giving 1,4-diketones selectively via one-electron oxidative desilylation.

Pentavalent $VO(OR)Cl_2$ is revealed to be a Lewis acid with one-electron oxidation capability, which has been demonstrated to be useful in oxidative transformations of carbonyl compounds. Cyclobutanones and diketene undergo one-electron oxidative ring opening to generate radical species at the γ or α position of the carbonyl group, respectively.[1] One-electron oxidation of organosilicon compounds accompanied by desilylation is considered to be synthetically potential in radical reactions. We herein report a versatile method for the selective and oxidative coupling of silyl enol ethers via β-oxo alkyl radicals.

The silyl enol ether **1** was treated with $VO(OEt)Cl_2$ in dichloromethane to give the symmetrical 1,4-diketone **2** (eq. 1). The results are summarized in Table 1. The reaction proceeded at a lower temperature as compared with other known metal oxidants[2] although depending on the starting silyl enol ethers. In contrast to the facile coupling of **1a**, **1d** was scarcely oxidized under the similar conditions. Only a small amount of the coupling product **2d** was obtained even when the reaction temperature was raised to room temperature.



The difference in reactivities is successfully applicable to the selective cross-coupling for the synthesis of unsymmetrical 1,4-diketones (eq. 2, Table 2).

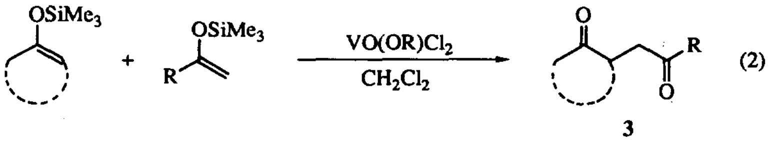
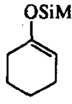
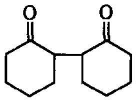
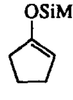
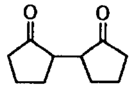
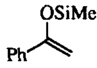
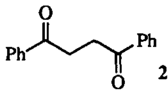
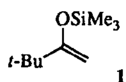
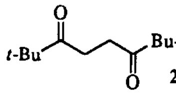


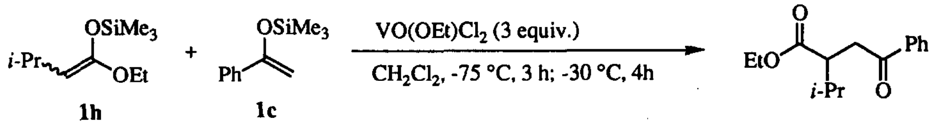
Table 1. Oxidative Coupling to Symmetrical 1,4-Diketones [a]

Silyl Enol Ether **1**	Conditions	1,4-Diketone **2**	Yield, %
 **1a**	-75 °C, 3 h; - 40 °C,4 h	 **2a**	74
 **1b**	-75 °C, 3 h; - 40 °C,4 h	 **2b**	88
 **1c**	-75 °C, 3 h; - 40 °C,4 h	 **2c**	30
 **1d**	-75 °C, 3 h; - 40 °C,4 h	 **2d**	trace
	-75 °C, 2 h; room temp., 12 h		11

[a] $VO(OEt)Cl_2$ (2 equiv.); solvent, CH_2Cl_2.

The cross-coupled ketone **3a** was exclusively produced in the reaction of the silyl enol ether **1a** with **1c**.[3] The simultaneous addition of the silyl enol ethers scarcely affected the selectivity. Increase in the amount of VO(OEt)Cl2 raised the yield of **3a**. VO(OPr-*i*)Cl2 worked similarly in the present oxidation. The selective synthesis of unsymmetrical 1,4-diketones is dependent on the substituent of silyl enol ethers. More substituted silyl enol ethers were susceptible to be oxidized. It should be noted that the regioselective carbon-carbon bond formation was observed in the case of **1f** and **1g**.

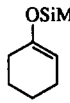
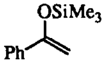
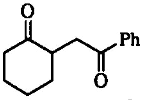
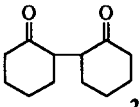
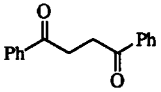
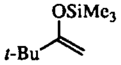
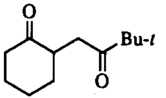
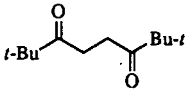
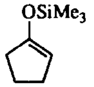
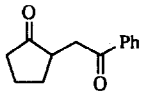
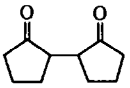
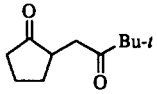
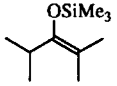
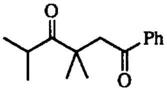
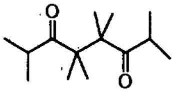
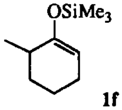
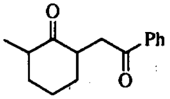
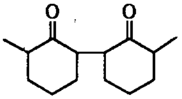
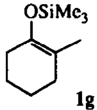
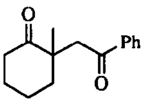
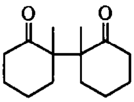
The silyl ketene acetal **1h** was also allowed to undergo the facile selective oxidation with VO(OEt)Cl2 to the γ-keto ester **3h**, being contaminated by only trace amounts of the homo-coupled products (eq. 3).



1h **1c** **3h** 94 % (3)

The silyl enol ether **1a** was converted to 2-bromocyclohexanone (37% yield) on treatment with VO(OEt)Cl2 (2 equiv.) and CBrCl3 (5 equiv.), indicating that a radical species is generated at the α-position of the carbonyl group. A plausible reaction course is explained as follows. One-electron oxidation of the silyl enol ether **1** with oxovanadium(V) species leads to the cation radical **4**, which undergoes desilylation to generate the radical **5**.[4] Cross-coupling is achieved by the selective intermolecular addition of **5** towards the second silyl enol ether. The adduct **6** is further oxidized with oxovanadium(V) species into the cation **7** followed by desilylation with formation of the 1,4-diketone **3** (Scheme 1).

Table 2. Oxidative Coupling to Unsymmetrical 1,4-Diketones[a]

Silyl Enol Ethers		VO(OR)Cl_2		1,4-Diketones[c] Yield, %		
1 equiv.	2 equiv.	R	equiv.			
 1a	 1c			 3a	 2a	 2c
		Et	1	31	trace	trace
		Et	2	50	trace	trace
		Et	3	67 (65)	trace	trace
		Et	3[b]	68	3	trace
		i-Pr	3	50	trace	trace
1a	 1d	Et	3	 54 (40)	2a 38	 trace 2d
 1b	1c	Et	3	 67 (62)	 trace 2b	2c trace
1b	1d	Et	3	 66 (58)	2b 32	2d trace
 1e	1c	Et	3	 93 (91)	 trace	2c trace
 1f	1c	Et	3	 77 (69)	 trace	2c trace
 1g	1c	Et	3	 49 (40)	 trace	2c trace

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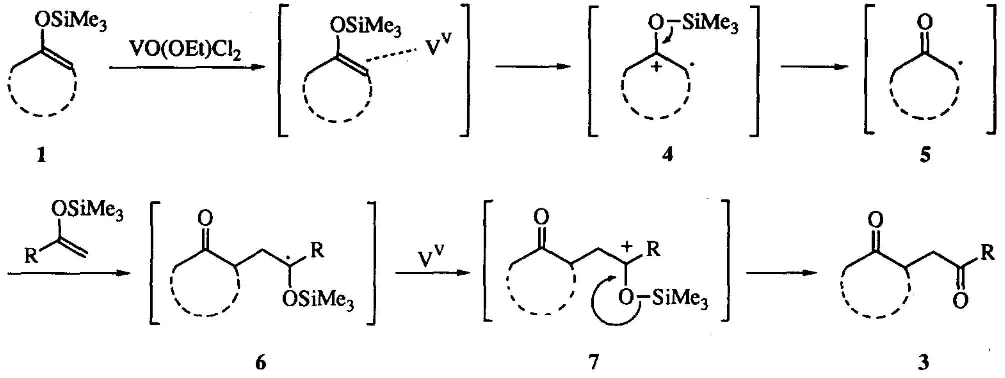
[a] Silyl enol ethers were stepwise added as described in ref. 3, unless otherwise stated. Solvent, CH_2Cl_2; -75 °C, 3 h then -30 °C, 4h.

[b] Silyl enol ethers were charged simultaneously.

[c] The numbers in parentheses are the isolated yields.

Scheme 1



Desilylation of silyl enol ethers by the oxovanadium(V) compound is considered to be based on the difference of their redox potential,[5] which permits the selective cross-coupling reaction. The present results indicate that the oxovanadium(V) compound is versatile to cleave the silicon-oxygen bond via selective one-electron oxidation. Further investigation on oxidative desilylation is now in progress.

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References and Notes

1. Hirao, T.; Fujii, T.; Miyata, S.-I.; Ohshiro, Y. *J. Org. Chem.* **1991**, *56*, 2264; Hirao, T.; Fujii, T.; Ohshiro, Y. *J. Organometal. Chem.* **1991**, *407*, C1.
2. Ito, Y.; Konoike, T.; Saegusa, T. *J. Am. Chem. Soc.* **1975**, *97*, 649; Kobayashi, Y.; Taguchi, T.; Morikawa, T.; Tokuno, E.; Sekiguchi, S. *Chem. Pharm. Bull.* **1980**, *28*, 262; Baciocchi, E.; Casu, A.; Ruzziconi, R. *SYNLETT* **1990**, 679.
3. A general experimental procedure is as follows. To a solution of $VO(OEt)Cl_2$ (3.0 mmol) in dichloromethane (4 mL) was added the silyl enol ether (2.0 mmol) at -75 °C, followed by the dropwise addition of the more reactive silyl enol ether (1.0 mmol) over 20 min. The resultant mixture was stirred at -75 °C for 3 h and then at -30 °C for 4 h. At the same temperature, 5% aqueous $Na_2S_2O_3$ (0.5 mL) and ether (10 mL) were added to the reaction mixture, which was extracted with ether (2 x 20 mL) followed by addition of conc. HCl (0.5 mL) and extraction with ether (3 x 20 mL). The combined ethereal solution was washed with saturated aqueous $NaHCO_3$ and brine, dried, and concentrated. The residue was chromatographed on a silica gel colomn to give the desired 1,4-diketone.
4. Another reaction path is invoked by one-electron oxidation of the oxovanadium enolate intermediates via transmetallation.
5 Fukuzumi, S. unpublished results.

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