

Novel Stereocontrolled Syntheses of Exocyclic γ -Oxovinyltrimethylsilanes. A Potential Route for Stereodefined Exocyclic Tetrasubstituted Alkenes

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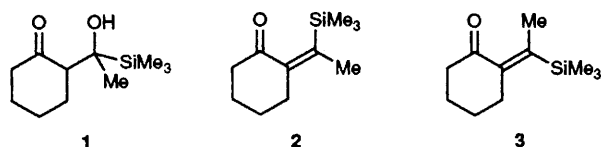
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The course of the dehydration of α -hydroxy- γ -oxotrimethylsilanes is highly dependent on the conditions to produce stereoselectively (*Z*)- and (*E*)- γ -oxovinyltrimethylsilanes, which are potential precursors for preparation of stereodefined exocyclic tetrasubstituted alkenes.

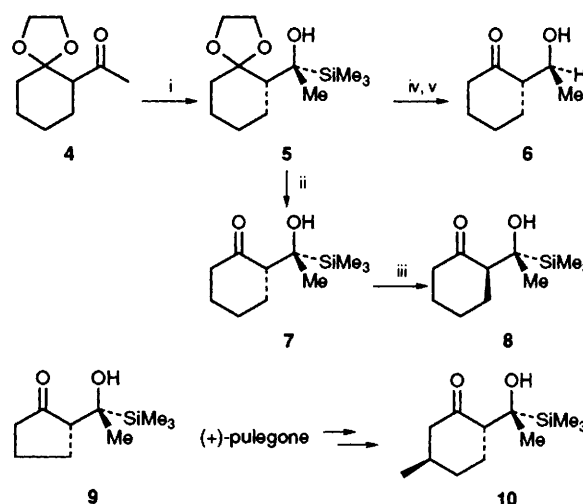
Even in modern synthetic organic chemistry, stereocontrolled syntheses of exocyclic tetrasubstituted alkenes are the subject of intensive investigations.^{1,2} Sequences involving *syn*-selective intramolecular carbometallation of alkynes followed by trapping the resulting α -metalloalkylidene species have met with success,³ while such sequences were expected to be dependent on the size of the ring formed in the intramolecular carbometallation. Alternative sequences involve the preparation of stereodefined exocyclic α -metalloalkylidene species from cyclic precursors, but methodologies for preparation of such species are not well established yet. We now describe preliminary results on novel stereocontrolled syntheses of (*Z*)- and (*E*)- γ -oxovinyltrimethylsilanes (e.g. **2** and **3**), potential equivalents of α -metalloalkylidene species, via dehydration of α -hydroxy- γ -oxotrimethylsilanes (e.g. **1**) derived from cycloalkanones.‡ The potential utility of the α -metalloalkylidene species was demonstrated by the conversion of **2** into the stereodefined exocyclic tetrasubstituted alkene **19**.

The synthesis of α -hydroxy- γ -oxotrimethylsilanes **7** and **8** (Scheme 1) is representative of a general procedure. Thus, addition of Me_3SiLi^4 to ketone **4**, obtained from either ethyl 2-oxocyclohexanecarboxylate in four steps or 2-acetylcyclohexanone by monoacetalization, exclusively produced α -hydroxytrimethylsilane **5**. Acid hydrolysis of the acetal moiety in **5** afforded *threo*- α -hydroxy- γ -oxotrimethylsilane **7**, whose stereochemistry was determined via conversion of **5** into the known *threo*-aldol **6**.^{5,6} The *erythro*-isomer **8**, on the other hand, was obtained by base-induced isomerization of **7**. Two other *threo*- α -hydroxy- γ -oxotrimethylsilanes **9** and **10** were similarly prepared from ethyl 2-oxocyclopentanecarboxylate and (+)-pulegone,[§] respectively. With α -hydroxy- γ -oxotrimethylsilanes in hand, we then examined their dehydration reaction to obtain γ -oxovinyltrimethylsilanes. The results of the dehydration are summarized in Table 1.

Under the standard $\text{MeSO}_2\text{Cl-Et}_3\text{N}$ conditions for dehydration of β -hydroxy ketones (entry 1), dehydration of **7** slowly gave (*Z*)- γ -oxovinyltrimethylsilane **2** and *trans* (*E*)-isomer **3** with low selectivity, accompanied by the methylene compound **11**. Stereochemical assignments of products were



primarily determined from the chemical shifts of both the vinyl methyl and the methyl group on silicon,¶ and were confirmed by NOE results for alcohol **18** derived from **2** (Fig. 1); preliminary results of an X-ray analysis of alcohol **18** derived from **2** supported these assignments. Use of excess reagents (entry 2) increased the reaction rate and gave **3** predominantly. On the other hand, with less Et_3N (entry 3) the product ratio dramatically changed to give **2** as the major product. Since the reaction medium seemed to become acidic by formation of $\text{Et}_3\text{N}\cdot\text{HCl}$ and/or $\text{Et}_3\text{N}\cdot\text{MeSO}_2\text{H}$ as the dehydration proceeded, acid catalysts were assumed to be effective for this dehydration. Thus, treatment of **7** with either camphorsulfonic acid (CSA) or pyridinium toluene-*p*-sulfonate (PPTS) afforded **2** with high (*Z*)-selectivity (94 : 6–95 : 5) (entries 4 and 5). Under acidic conditions, the methylene compound was not detected. In the case of **8** with an *erythro*-configuration, $\text{MeSO}_2\text{Cl-Et}_3\text{N}$ conditions afforded **2** as the predominant product (entry 6, cf. entry 2). Under acidic conditions (CSA), the dehydration of **8** required a prolonged reaction time and resulted in the production of **2** selectively (entry 7, cf. entry 4).|| Neither epimerization nor dehydration of **8** was detected



Scheme 1 Reagents and conditions: i, Me_3SiLi , hexamethylphosphoric triamide-tetrahydrofuran (HMPA-THF), -78°C , 55% (89% conv.) + diastereoisomer of **5** (2%); ii, PPTS, acetone- H_2O , reflux, 76%; iii, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), CH_2Cl_2 , room temp., 50% (77% conv.); iv, tetrabutylammonium fluoride (TBAF), dimethylformamide (DMF), room temp., 63% (93% conv.); v, PPTS, acetone- H_2O , reflux, 87%

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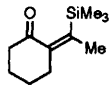
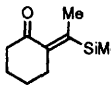
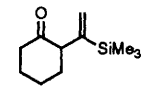
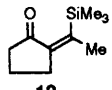
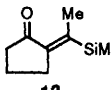
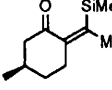
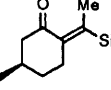
‡ To the best of our knowledge, neither preparation of α -hydroxy- γ -oxotrimethylsilanes nor their dehydration reactions have been reported.

§ Compound **10** was prepared via (9-methyl-1,4-dioxaspiro[4.5]decan-6-yl)ethanone derived from deconjugative acetalization of (+)-pulegone ($\text{HOCH}_2\text{CH}_2\text{OH}$, *p*- $\text{MeC}_6\text{H}_4\text{SO}_3\text{H}$, benzene, reflux with azeotropic removal of water) followed by ozonolysis of the resulting isopropenyl moiety.

¶ Selected ^1H NMR data (C_6D_6): **2**: δ 0.36 (s, 9H, SiMe_3) and 1.65 (s, 3H, Me); **3**: 0.07 (s, 9H, SiMe_3) and 1.99 (s, 3H, Me). The methyl signal on the same side as the carbonyl group was considered to be downfield.

|| Since epimerization of **8** into **7** under these conditions was observed on TLC analysis, the possibility that acid catalysed dehydration of **8** proceeded via **7** is conceivable.

Table 1 Dehydration of γ -oxo- α -hydroxytrimethylsilanes

Entry	Starting material	Reagent(s) (equiv.) and conditions in CH ₂ Cl ₂ ^f	Product ratio (isolated yield %) ^{a,b}		
					
1	7	MsCl (2), Et ₃ N (4.2), 0 °C, 27 h	10	31	9 ^c
2	7	MsCl (6), Et ₃ N (12.6), 0 °C, 3.5 h	6 (5)	66 (71) ^d	28
3	7	MsCl (2), Et ₃ N (2.2), 45 h	87 (65)	13 (14)	—
4	7	CSA (0.25), 0 °C, 4 h	94 (73)	6 (7)	— ^e
5	7	PPTS (0.25), 106 h	95 (73)	5 (6)	—
6	8	MsCl (6), Et ₃ N (12.6), 0 °C, 1.5 h	69	3	29
7	8	CSA (0.25), 0 °C, 44 h	91	9	—
8	9	PPTS (0.25), 406 h			—
9	9	MsCl (6), Et ₃ N (12.6), 0 °C, 1 h	7	81	12
10	10	CSA (0.25), 9 h			—
11	10	MsCl (6), Et ₃ N (12.6), 0 °C, 1 h	3	70	24

^a Ratio was determined by GLC analysis. ^b Figures in parentheses are isolated yields. ^c Remainder, recovery of starting material. ^d Combined yield of 3 and 11 owing to difficulties in their separation. ^e 8 (5%) formed by isomerization of 7 was isolated. ^f Room temp. unless otherwise noted. Ms = MeSO₂.

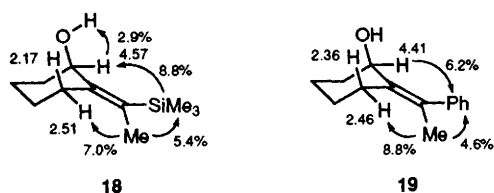


Fig. 1 NOEs for 18 and 19

on treatment with PPTS as the acid catalyst. The dehydrations of 9 and 10 were similarly dependent on the reaction conditions to give either the (*Z*)-isomers 12 and 15 on acid treatment (entries 8 and 10) or the (*E*)-isomers 13 and 16 under MeSO₂Cl-Et₃N conditions (entries 9 and 11) as predominant products, respectively.

Dehydration with MeSO₂Cl-Et₃N is stereospecifically *anti*, although not completely. On the other hand, with acid catalysts the dehydration of both 7 and 8 proceeded stereoselectively giving 2. The ratios of 2 and 3 determined at an early stage in the dehydrations of 7 and 8 with CSA were 74:7 (1 h at 0 °C, conv. 80%) and 57:5 (4 h at 0 °C, conv. 60%), respectively. Since these ratios were close to those of the final products (*cf.* entries 4 and 7), the (*Z*)-isomer 2 was considered to be the kinetically favourable product under acidic conditions. Furthermore equilibration studies showed

that in the presence of acid, 2 was thermodynamically more stable than 3. Thus, upon treatment of pure 2 and 3 with CSA separately at room temperature, the ratios of 2 and 3 in the mixtures obtained were nearly identical (90:10 and 85:15). This thermodynamic stability of the (*Z*)-isomer might be rationalized by the weak coordination of the carbonyl oxygen to the silicon atom in the Me₃Si group as depicted in **i** (Fig. 2). In the ²⁹Si NMR spectra, a small upfield shift of silicon in 2 (δ -7.0) compared to that in 3 (δ -4.9) was observed although the IR spectra of 2 and 3 did not provide evidence for such coordination.^{7**}

** It is known that it is essential for such intramolecular coordination (O→Si) that silicon should have at least one electronically negative substituent. Accordingly, it might be assumed that the α,β -unsaturated- γ -carbonyl moiety in 2 was consistent with this requirement. See: A. I. Alabanov, L. I. Gubanov, M. F. Larin, V. A. Pestunovich and M. G. Voronkov, *J. Organomet. Chem.*, 1983, **244**, 5, and references therein.

The thermodynamic stability of the (*Z*)-isomer may also be accounted for by considering the transient stabilization of the extended enol form *via* partial donation of electron density from oxygen to silicon as indicated in **ii**. Contrary to these experimental results, MOPAC PM3 calculations (ver. 6.01, Cache system, SONY Tektronix) showed that the (*E*)-isomer 3 was more stable than the (*Z*)-isomer 2 comparing their heats of formation: 2, -85.89 kcal mol⁻¹; 3, -86.89 kcal mol⁻¹ (1 cal = 4.184 J).

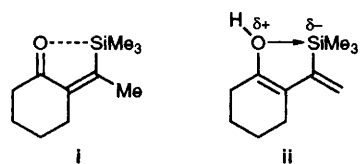
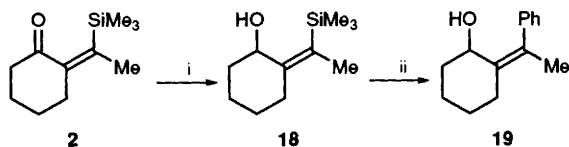


Fig. 2



Scheme 2 Reagents and conditions: i, diisobutylaluminium hydride (DIBAL), CH_2Cl_2 , -78°C , 98%; ii, PhI, TBAF, $\{[\text{Pd}(\eta^3\text{-C}_3\text{H}_5)\text{Cl}]_2\}$ (0.02 equiv.), DMF, 50°C , 60%

The vinyltrimethylsilyl moieties in those γ -oxovinyltrimethylsilanes were expected to participate in various types of reactions developed for conventional vinylsilanes.⁸ Their potential utility as α -metalloalkylidene species was demonstrated by conversion into stereodefined exocyclic tetrasubstituted alkenes *via* γ -hydroxyvinylsilane (Scheme 2). Thus, according to the literature,⁹ (*Z*)- γ -hydroxyvinylsilane **18** obtained by reduction of **2** with DIBAL was treated with iodobenzene in the presence of Pd^{II} catalyst and TBAF to produce **19** as the sole product in 60% yield.¹⁰ The purity of **19** was determined by ^1H NMR as well as HPLC analyses and its (*Z*)-stereochemistry was unambiguously confirmed by NOE difference spectra (Fig. 1). In spite of the low reactivity of vinyltrimethylsilanes,^{9b} the production of the exocyclic tetrasubstituted alkenes from sterically congested trisubstituted vinylsilanes is worth noting. Participation of the γ -hydroxy group in the cross coupling reaction was strongly suggested by the observation that the (*E*)-isomer of **18** as well as oxovinylsilanes **2** and **3** were inert under these conditions.

In conclusion, we have developed novel stereoselective syntheses of exocyclic (*E*)- and (*Z*)- γ -oxovinyltrimethylsilanes *via* dehydration of α -hydroxy- γ -oxotrimethylsilanes. The observed (*Z*)-selectivity in the acid catalysed dehydration reaction might be rationalized by the interaction of carbonyl oxygen with silicon, which was expected to be enhanced by introducing electronically more negative substituents than the methyl group on silicon.¹¹ Such substituents were also expected to accelerate the reaction rate of the fluoride induced palladium catalysed coupling reaction.⁹

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