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

Kazuhiko Nakatani,*†ª Tomoko Izawa,ª Yoshihiko Odagaki ^b and Sachihiko Isoe* ^a

Institute of Organic Chemistry, Faculty of Science, Osaka City University, 3-3-138, Sugimoto, Sumiyoshi, Osaka 558, Japan

^b Minase Research Laboratories, ONO Pharmaceutical Co. Ltd, Mishima, Osaka 618, Japan

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 Me₃SiLi⁴ 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 y-oxovinyltrimethylsilanes. The results of the dehydration are summarized in Table 1.

Under the standard MeSO₂Cl-Et₃N conditions for dehydration of β -hydroxy ketones (entry 1), dehydration of 7 slowly gave (Z)- γ -oxovinyltrimethylsilane 2 and tis (E)-isomer 3 with low selectivity, accompanied by the methylene compound 11. Stereochemical assignments of products were



† Present address: Department of Synthetic Chemistry and Biological Chemistry, Faculty of Engineering, Kyoto University, Kyoto 606-01, Japan.

 \ddagger 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 (HOCH₂CH₂OH, *p*-MeC₆H₄SO₃H, benzene, reflux with azeotropical removal of water) followed by ozonolysis of the resulting isopropenyl moiety. 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 Et₃N (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 Et₃N·HCl and/or Et₃N·MeSO₃H 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, MeSO₂Cl-Et₃N 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, Me₃SiLi, hexamethylphosphoric triamide-tetrahdyrofuran (HMPA-THF), -78 °C, 55% (89% conv.) + diastereoisomer of 5 (2%); ii, PPTS, acetone-H₂O, reflux, 76%; iii, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), CH₂Cl₂, room temp., 50% (77% conv.); iv, tetrabutylammonium fluoride (TBAF), dimethylformamide (DMF), room temp., 63% (93% conv.); v, PPTS, acetone-H₂O, reflux, 87%

¶ Selected ¹H NMR data (C_6D_6): 2: δ 0.36 (s, 9H, SiMe₃) and 1.65 (s, 3H, Me); 3: 0.07 (s, 9H, SiMe₃) 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.

| | | | Product ratio (isolated yield %) ^{a,b} | | | |
|-------|----------------------|---|---|---------------------------|-------------------|--|
| Entry | Starting material | Reagent(s) (equiv.) and conditions in CH ₂ Cl ₂ ^r | 2 SiMe ₃ Me | SiMe ₃ | SiMe ₃ | |
| 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) | _ ° | |
| 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 | - | |
| | | | O SiMe ₃ | O Me | î | |
| | | | Me | SiMeg | SiMe ₃ | |
| | | | 12 | 13 | 14 | |
| 8 | 9 | PPTS (0.25), 406 h | 82 | 18 | - | |
| 9 | 9 | MsCl (6), Et ₃ N (12.6), 0 °C, 1 h | 7 | 81 | 12 | |
| | | | O SiMe ₃ Me | O Me SiMe ₃ | SiMe ₃ | |
| | | | 15 | 16 | 17 | |
| 10 | 10 | CSA (0.25), 9 h | 92 (76) | 8 (4) | - | |
| 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. $Ms = MeSO_2$.



on treatment with PPTS as the acid catalyst. The dehdyrations 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 antialthough 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 $(O \rightarrow Si)$ that silicon should have at least one electronically negative substituent. Accordingly, it might be assumed that the α , β -unsaturated-y-carbonyl moiety in 2 was consistent with this requirement. See: A. I. Alabanov, L. I. Gubanova, 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).





The vinyltrimethylsilyl moieties in those y-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 y-hydroxyvinylsilane (Scheme 2). Thus, according to the literature, P(Z)- γ -hydroxyvinilsilane 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 y-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 oxgen 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 1367

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