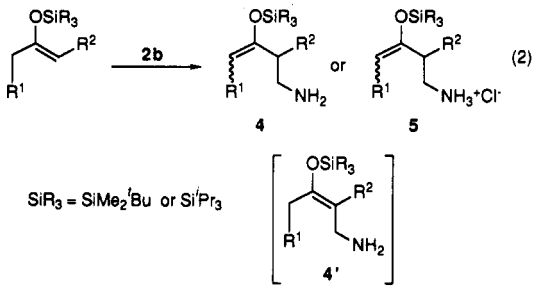

could not be detected, even in the reactions of enol ethers with no α'-hydrogen. For example, the reaction with the enol ether of acetophenone gave a rather complex mixture, from which β-(*N*-benzoylamino)propiophenone alone was isolated in moderate yield following treatment with benzoyl chloride.[9] These features contrast nicely with those of reactions with $Me_2N{=}CH_2I$.[12] The stereochemical outcome has also been examined using 3- or 4-substituted cyclohexanone derivatives. The former preferentially produced trans adduct (entry 4),[13] whereas selectivity was lower with the latter (entry 5, Table I).

Interestingly, workup with a buffer solution (pH = 7.4) rather than aqueous sodium hydroxide gave the corresponding hydrochloride **5** as white crystalline compounds. No isomerization of the double bond was observed except in the case of the cycloheptanone derivative (entry 2, Table I).

The stereoselectivity exhibited in entry 5 of Table I provides information concerning the reaction mechanism. A concerted ene reaction of 4-alkyl-1-siloxycyclohexene should give the trans product via axial attack of **2b**, because the cyclic transition-state structure[14] of the ene reaction requires abstraction of an axial α'-hydrogen. Judging from the stereoselectivity in entry 5, which is as low as that of the reaction of the 4-substituted enol ether with a Lewis acid activated electrophile,[15] the stepwise reaction mechanism seems more plausible.

The products **4** containing the enol silyl ether moiety as well as the primary amino group show promise for use in the construction of heterocycles via regioselective C–N and C–C bond formation.

We are currently studying synthetic applications of **4** and the reactions of **2a,b** with various kinds of nucleophiles.

Acknowledgment. This work was partially supported by Grants from the Ministry of Education, Science, and Culture of the Japanese Government.

Supplementary Material Available: Experimental procedures and spectral data of **4** and **5** (3 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(11) Typical procedure is as follows: To a suspension of $AlCl_3$ (73 mg, 0.55 mmol) in CH_2Cl_2 (1.5 mL) was added (trimethylsilyl)methyl azide (82 μL, 0.55 mmol) at −45 °C, and the mixture was stirred at this temperature for 1 h and then at 0 °C for 0.5 h and finally at room temperature for 0.5 h. The resulting solution was cooled to −10 °C, and to this was added 0.50 mmol of enol silyl ether. After 10–40 h at −10 °C, aqueous sodium hydroxide was added. Usual workup followed by silica gel chromatography gave the enol silyl ether of β-amino ketone.

(12) The reaction of $Me_2N{=}CH_2I$ with 1-(*tert*-butyldimethylsiloxy)-cyclohexene gave 2-(aminomethyl)-1-siloxycyclohexene as a sole product: Wada, M.; Nishihara, Y.; Akiba, K. *Tetrahedron Lett.* **1984**, *25*, 5405. See also: Danishefsky, S.; Kitahara, T.; McKee, R.; Schuda, P. F. *J. Am. Chem. Soc.* **1976**, *98*, 6715.

(13) In contrast to the high regioselectivity observed in the reaction with **2b**, $Me_2N{=}CH_2I$ seems to induce the isomerization of the double bond of 3-methyl-1-(triisopropylsiloxy)cyclohexene under the reaction conditions to afford a mixture of two regioisomers.

(14) Loncharich, R. J.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 6947.

(15) For example, treatment of 4-*tert*-butyl-1-(trimethylsiloxy)cyclohexene with chloromethyl phenyl sulfide under the influence of $TiCl_4$[16] afforded 4-*tert*-butyl-2-[(phenylthio)methyl]cyclohexanone as a mixture (63:37) of diastereoisomers.

(16) Paterson, I.; Fleming, I. *Tetrahedron Lett.* **1979**, 993.

Cyclizations of Functionalized Acylsilanes To Form 2-Silyldihydropyrans and 2-Silyldihydrofurans

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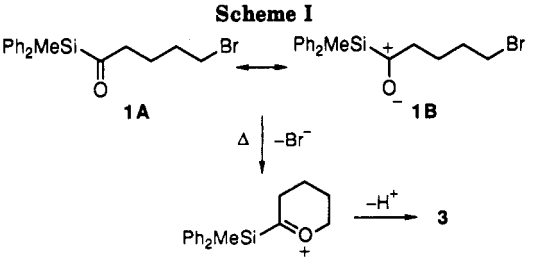
Summary: Cyclizations of (δ-haloacyl)- and (γ-haloacyl)silanes in a polar aprotic solvent gave 2-silyldihydropyrans and 2-silyldihydrofurans in good yields. This new type of cyclization could also be initiated by a carbocation and an olefin.

Acylsilanes are a useful class of compounds in organic synthesis.[1,2] Much of the attention paid to the chemistry of acylsilanes has been focused on the electrophilic reaction of the carbonyl carbon. In this report, we wish to address the previously ignored nucleophilic nature of the carbonyl oxygen.

In a project exploring the radical chemistry of acylsilanes, we prepared (bromoacyl)silane **1**[3] via silylation of

Scheme I



1,3-dithiane[4,5] followed by alkylation with 1,4-dibromobutane and hydrolysis.[6] Although bromide **1** is stable in refluxing benzene overnight, we found that heating **1** in

(1) Ricci, A.; Degl'Innocenti, A. *Synthesis* **1989**, 647.

(2) Page, P. C. B.; Klair, S. S.; Rosenthal, S. *Chem. Soc. Rev.* **1990**, *19*, 147.

(3) Tsai, Y.-M.; Cherng, C.-D. *Tetrahedron Lett.* **1991**, *32*, 3515.

(4) Brook, A. G.; Duff, J. M.; Jones, P. F.; Davis, N. R. *J. Am. Chem. Soc.* **1967**, *89*, 431.

(5) Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1967**, *89*, 434.

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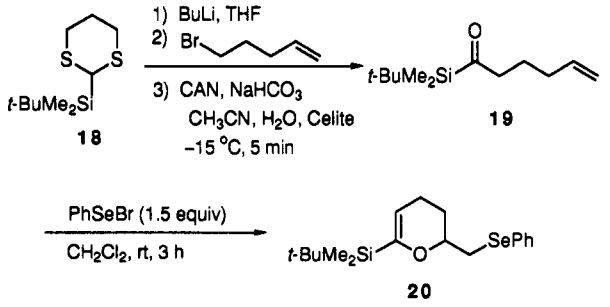
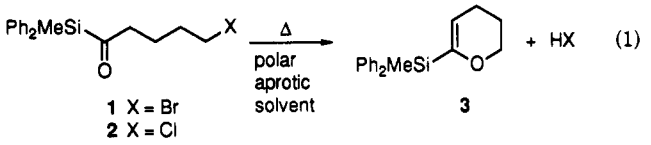
Scheme II



a polar aprotic solvent under nitrogen led to the formation of 2-silyldihydropyran **3** (eq 1).



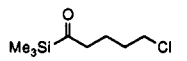
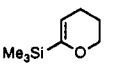
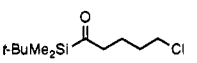
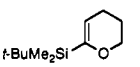
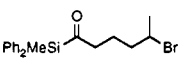
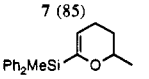
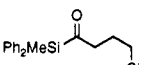
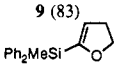
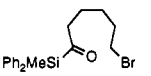
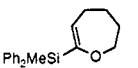
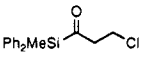
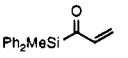
Acylsilanes are well known to have a significant contribution from dipolar resonance structures such as **1B** (Scheme I).[2] It is generally believed that electron donation from the silicon atom toward the carbonyl group stabilizes the dipolar structure. This special property translates into the unusual electrophilicity of the carbonyl carbon of acylsilanes. Yates and Agolini have reported the remarkable basicity of acylsilane carbonyl groups.[7] The basicity indicates that the electron density on the carbonyl oxygen is higher than that of normal ketones. Therefore, we believe that the cyclization process leading to **3** is probably initiated by the attack of the carbonyl oxygen to displace the bromide and subsequent loss of a proton. The fact that the cyclization occurs demonstrates the significance of the nucleophilic nature of the carbonyl oxygen of acylsilanes.

As shown in Table I, the best result was obtained when *N*-methyl-2-pyrrolidinone (NMP) was used as the solvent (entry 1). Among the other commonly used polar solvents, DMF also worked well (entry 3). However, the reaction appeared to be sluggish in acetonitrile and THF (entries 5–8). Only decomposition of starting material was observed in DMSO, possibly due to the nucleophilic attack of the DMSO-oxygen on the acylsilane (entry 9). Note that **3** was unusually stable in the presence of hydrogen bromide. The cyclization reaction could also be performed in the presence of 1 equiv of triethylamine to remove the acid byproduct (entries 2, 4). Although the reaction rate appeared to be faster in the presence of triethylamine, the yield was slightly lowered.

We next turned our attention to (chloroacyl)silane **2**, which could be prepared in much better yield than the bromide.[3] As shown in entry 10, the chloride was less reactive (entry 10). However, with the addition of anhydrous potassium iodide, the reaction could be performed in excellent yield (entry 14).

The reason that we chose acyldiphenylmethylsilane for our study was purely for the convenience of the isolation of the product, which contains a chromophore and is less volatile than the products obtained from other acylsilanes. The cyclization also worked well for acyltrimethylsilane **4** (entry 15) and acyl-*tert*-butyldimethylsilane **6** (entry 16). The lower yield of **5**[8] was due to the volatility of this compound. With a secondary bromide (entry 17), the cyclization required less time. In contrast to the reaction of **1**, the reaction of **8** in refluxing benzene (6 h) afforded a small amount of **9** (5%).

Table I. Cyclizations of Halo Acylsilanes

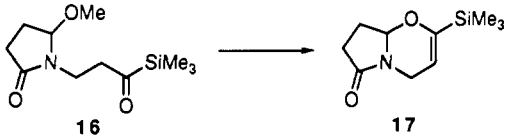
entry	substrate[a]	solvent (addend)[b]	temp (°C)	time (h)	product (% yield)[c]
1	**1**	NMP	100	13	**3** (91)
2	**1**	NMP (Et3N, 1 equiv)	100	6	**3** (79)
3	**1**	DMF	100	9	**3** (79)
4	**1**	DMF (Et3N, 1 equiv)	100	5	**3** (75)
5	**1**	CH3CN	80	23	**3** (42)
6	**1**	CH3CN (Et3N, 1 equiv)	80	48	**3** (55)
7	**1**	THF	67	7	no reaction
8	**1**	THF (Et3N, 1 equiv)	67	12	no reaction
9	**1**	DMSO	100	4	--
10	**2**	DMF	100	72	**3** (39)
11	**2**	DMF (KI, cat)	100	48	**3** (53)
12	**2**	DMF (KI, 1 equiv; Et3N, 1 equiv)	100	13	**3** (66)
13	**2**	NMP (KI, 1 equiv)	100	48	**3** (97)
14	**2**	NMP (KI, 2 equiv)	100	16	**3** (94)
15	 **4**	NMP (KI, 2 equiv)	90	20	 **5** (71)[d]
16	 **6**	NMP (KI, 1.8 equiv)	90	14	 **7** (85)
17	 **8**	NMP	100	9.5	 **9** (83)
18	 **10**	NMP (KI, 1 equiv)	66	30	 **11** (72)
19	**10**	NMP (KI, 3 equiv)	70	8	**11** (94)
20	 **12**	NMP	100	40	 **13** (trace)[e]
21	 **14**	NMP (NaBr, 1.5 equiv; EtBr, 30 equiv)[f]	60	30	 **15** (50)

[a] Prepared by silylation of 1,3-dithiane followed by alkylation with suitable dihalides and then hydrolysis (red HgO, BF_3·OEt_2). [b] Anhydrous solvents and reagents were used. [c] Products were purified by column chromatography. [d] Purified by Kugelrohr distillation (ref 8). [e] The presence of **13** was based on the characteristic ^{1}H NMR (200 MHz; $CDCl_3$) signals at δ 5.3 (t, J = 6 Hz, 1 H, vinyl) and 3.8 (t, J = 5 Hz, 2 H, OCH_2). [f] Reference 9.

(7) Yates, K.; Agolini, F. *Can. J. Chem.* **1966**, *44*, 2229–2231.
(8) Rautenstrauch, V. *Helv. Chim. Acta* **1972**, *55*, 594.

The cyclization is not limited to the formation of dihydropyrans. Dihydrofuran 11[9] (entry 19) could also be obtained. We found that 11 was more sensitive to the hydrogen halides and that a higher reaction temperature resulted in a lower yield. Therefore, using more potassium iodide to shorten the reaction time was crucial to ensure a better yield. Unfortunately, this method was not useful for seven-membered ring formation (entry 20). In another experiment, using modified Finkelstein reaction conditions,[10] acylsilane 14 gave only α,β-unsaturated acylsilane 15 (entry 21).

It is not necessary to use (haloacyl)silane in this type of cyclization. When an acyliminium ion was generated from 16[11] (eq 2), it could be trapped by the acylsilane to



(2)

16 17

conditions:	% yield
CH_3CN, rt, CSA (cat), 7 h	81
THF, rt, CSA (cat), 11 h	77
CH_2Cl_2, rt, CSA (cat), 8 h	62

*CSA: camphorsulfonic acid

give the interesting heterocycle 17 in good yields under very mild conditions.

We have also synthesized δ,ϵ-unsaturated acylsilane 19 (Scheme II) via alkylation of 18[12] (85%) followed by hydrolysis (70%) with ceric ammonium nitrate (CAN).[13-15] Treatment of 19 with phenylselenyl bromide at room temperature gave dihydropyran 20 in 72% yield. This cyclization reaction is a new addition to the family of olefin-initiated cyclization processes.[16]

In summary, this new cyclization method provides easy access to 2-silyldihydropyrans and 2-silyldihydrofurans from acylsilanes.[17] Previously, these types of compounds were prepared by lithiation of dihydropyrans or dihydrofurans followed by silylation.[8,9] Our method provides a versatile alternative through which compounds bearing a variety of substituents, such as 17 and 20, can be prepared. The special substitution pattern at C-2 and C-3 in the cyclization products affords a handle for further manipulations that may be useful in the synthesis of polyether antibiotics.[18]

Acknowledgment. Financial support by the National Science Council of the Republic of China is gratefully acknowledged (Grant 81-0208-M002-01).

Supplementary Material Available: Experimental procedures for the cyclizations, preparation of compounds 4, 6, 8, 10, 12, 14, 19, and 20, and spectroscopic data for new compounds 1-4, 6-17, 19 and 20 (9 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(9) Lukevics, E.; Gevorgyan, V. N.; Goldberg, Y. S.; Shymanska, M. V. *J. Organomet. Chem.* **1985**, *294*, 163.
(10) Willy, W. E.; McKean, D. R.; Garcia, B. A. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1989.
(11) The preparation of 16 will be reported elsewhere.
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A New and Efficient Asymmetric Synthesis of an A-Ring Precursor to Physiologically Active 1α-Hydroxyvitamin D_3 Steroids

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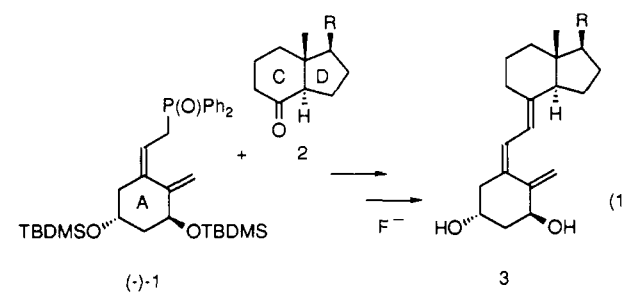
Summary: A highly stereocontrolled and mild Diels-Alder cycloaddition involving stereochemically matched pyrone (*S*)-lactate 4 and Lewis acid (−)-Pr(hfc)$_3$ produced bicyclic lactone *endo*-5 via a double stereodifferentiation process. Bicyclic lactone 5 was then transformed smoothly and in high yield into phosphine oxide (−)-1, an important A-ring precursor to various physiologically active 1α-hydroxyvitamin D_3 steroids.

Lythgoe-type (i.e., Horner–Wittig)[2] coupling of the conjugate base of the A-ring phosphine oxide (−)-1 with C,D-ring units 2 carrying various side-chain groups R (eq 1) is one of the most popular and reliable methods currently used to prepare 1α-hydroxyvitamin D_3 compounds having desirable medicinal properties, such as separation



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(2) (a) Lythgoe, B. *Chem. Soc. Rev.* **1980**, 449. (b) Kocienski, P. J.; Lythgoe, B. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1440. (c) For a review of synthetic methods, see: Kametani, T.; Furayama, H. *Med. Res. Rev.* **1987**, *7*, 147.

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