herein contrast sharply to the copper-promoted cross-coupling reactions[3b] wherein homo coupling often results considerably. Also, vinylation of aryl compounds catalyzed by transition-metal complexes frequently lacks regiospecificity and is accompanied by considerable homo coupling products of both substrates.[17]

Second, reaction conditions are so mild that, unlike many other similar reactions, the fluoride ion promoted cross-coupling using organosilanes is tolerant of a wide variety of organic functionality on both substrates: ester (entries 8 and 10) or ketone (entries 5 and 9) carbonyls, ethoxy (entry 17), hydroxy (entry 21), and even aldehyde carbonyl (entry 11). Thus, without protection of these groups, functionalized styrene, conjugated diene, and enyne derivatives are readily accessible by the one-pot reaction.

Third, stereospecificity and regioselectivity of the reaction is noteworthy. The reaction proceeds with retention of the double-bond geometry of the vinyl halides (entries 7 and 14). Further, the coupling reaction of allylsilane with cinnamyl bromide took place selectively at the primary allylic carbon of the bromide (entry 23).

In conclusion, the TASF/Pd catalyst promoted cross-coupling of organosilanes with organic halides has the advantage of stereospecificity and chemoselectivity in addition to commercial availability of organosilicon compounds and provides a facile method for the construction of the conjugated carbon systems.

Registry No. TASF, 59201-86-4; H_2C=CHTMS, 754-05-2; H_2C=CHCH=CHTMS, 1798-76-1; H_2C=C(TMS)OEt, 81177-92-6; (*E*)-PhCH=CHTMS, 19372-00-0; PhC≡CTMS, 2170-06-1; TMSC≡C-*n*-C_5H_{11}, 15719-56-9; $HOCH_2C$≡CTMS, 5272-36-6; H_2C=$CHCH_2$TMS, 762-72-1; *p*-IC_6H_4Me, 624-31-7; *p*-$IC_6H_4NO_2$, 636-98-6; *p*-$IC_6H_4NH_2$, 540-37-4; *p*-IC_6H_4Ac, 13329-40-3; *p*-IC_6H_4I, 624-38-4; (*E*)-ICH=CHC_6H_{13}, 42599-17-7; (*E*)-ICH=CH-$(CH_2)_8CO_2Me$, 78461-59-3; (*E*)-ICH=$CH(CH_2)_8Ac$, 104761-38-8; (*E*)-ICH=$CH(CH_2)_9OAc$, 111468-58-7; (*E*)-ICH=$CH(CH_2)_8CHO$, 111468-59-8; (*E*)-ICH=CHC(=CH_2)$(CH_2)_2Ph$, 111468-60-1; (*Z*)-ICH=CH-*n*-C_6H_{13}, 52356-93-1; (*E*)-ICH=CHPh, 42599-24-6; $BrCH_2CH$=CHPh, 4392-24-9; *p*-MeC_6H_4CH=CH_2, 622-97-9; *p*-$NO_2C_6H_4CH$=CH_2, 100-13-0; *p*-$NH_2C_6H_4CH$=CH_2, 1520-21-4; *p*-AcC_6H_4CH=CH_2, 10537-63-0; *p*-$(CH_2$=$CH)_2C_6H_4$, 105-06-6; (*E*)-H_2C=CHCH=CHC_6H_{13}, 58396-45-5; (*E*)-H_2C=CHCH=$CH(CH_2)_8CO_2Me$, 80625-41-8; (*E*)-H_2C=CHCH=$CH(CH_2)_8Ac$, 111468-61-2; (*E*)-H_2C=CHCH=$CH(CH_2)_9OAc$, 80625-42-9; (*E*)-H_2C=CHCH=$CH(CH_2)_8CHO$, 111468-62-3; (*E*)-H_2C=CHCH=CHC(=CH_2)$(CH_2)_2Ph$, 111468-63-4; (*Z*)-H_2C=CHCH=CH-*n*-C_6H_{13}, 66717-33-7; (*E*)-H_2C=CHCH=CHPh, 16939-57-4; H_2C=CHCH=CHCH=CH-*n*-C_6H_{13}, 72084-21-0; (*E*)-H_2C=C(OEt)CH=CHPh, 1902-98-3; (*E*,*E*)-PhCH=CHCH=CHPh, 538-81-8; (*E*)-PhC≡CCH=CHPh, 13343-79-8; (*E*)-*n*-$C_5H_{11}C$≡CCH=CHPh, 111468-65-6; (*E*)-$HOCH_2C$≡CCH=CHPh, 103606-73-1; (*E*)-H_2C=$CHCH_2CH$=CHPh, 55666-17-6; (*E*)-H_2C=$CH(CH_2)_2CH$=CHPh, 56644-04-3; (η^3-$C_3H_5PdCl)_2$, 12012-95-2; 1-iodonaphthalene, 90-14-2; 1-iodocyclohexene, 17497-53-9; 1-vinylnaphthalene, 826-74-4; 1-ethenylcyclohexene, 2622-21-1.

Supplementary Material Available: Physical and spectroscopic data for new compounds (4 pages). Ordering information is given on any current masthead page.

(17) (a) Heck, R. F. *Org. React. (N.Y.)* **1982**, *27*, 345. (b) Plevyak, J. E.; Heck, R. F. *J. Org. Chem.* **1978**, *43*, 2454. (c) Kikukawa, K.; Ikenaga, K.; Kono, K.; Toritani, K. *J. Organomet. Chem.* **1984**, *270*, 277.

Yasuo Hatanaka, Tamejiro Hiyama*

Sagami Chemical Research Center
4-4-1 Nishiohnuma, Sagamihara
Kanagawa 229, Japan

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Silyl Enol Ethers Bearing Stereogenic Silicon Atoms and Chiral Alkoxy Groups: The Effect of These Groups upon the Facial Selectivity of the Epoxidation of an Enol Double Bond[1]

Summary: Silyl enol ethers having stereogenic silicon atoms which bear chiral alkoxy groups on the silicon were prepared and found to induce modest stereoselectivity in MCPBA epoxidations of the enol double bond by virtue of the alkoxy group.

Sir: We recently reported that the lithium enolate of pinacolone reacted with dichlorodimethylsilane to form chlorosilyl enol ether **1** which underwent displacement reactions with alcohols and amines to yield alkoxysilyl and aminosilyl enol ethers (e.g. **2** and **3**, Scheme I).[2] We are interested in silyl enol ethers bearing non-alkyl ligands on the silicon because such ligands may electronically or sterically affect the reactivity of the enol ether, relative to that of the better-known trialkylsilyl ethers,[3] in a synthetically useful manner. A chiral alkoxy or amino group on the silicon may direct the approach of a reagent preferentially to one face of the prochiral enol ligand, and a stereogenic silicon atom in the silyl enol ether may also affect the stereoselectivity of such additions.[4] To our knowledge, only one report of silyl enol ethers bearing stereogenic silicon atoms—a series of β-dicarbonyl-derived enol ethers bearing the well-known chiral methylphenyl-α-naphthylsilyl group—is in the literature.[5] Our methodology is well-suited to the synthesis of a great variety of chiral enol ethers, as the reaction of a lithium enolate with a dichlorosilane bearing any two different alkyl groups will form a chlorosilyl enol ether which would react with a chiral alcohol or amine to form diastereomeric enol ethers epimeric at the silicon. We now report the first syntheses of alkoxysilyl enol ethers which are chiral at the silicon center and results of a study of the effects of a chiral alkoxy group and a stereogenic silicon atom upon the stereofacial selectivity of a peracid epoxidation of one of these silyl enol ethers.

A list of enol ethers that we have prepared is given in Table I. When lithium enolates were exposed to dichloromethylphenylsilane followed by (*S*)-methyl mandelate, alkoxysilyl enol ethers **4a,b**, **5a,b**, and **6a,b** were formed in high yields.[6] The diastereomers could be separated by using preparative HPLC to yield enantiomerically pure silyl ethers. Varying the chiral alcohol to (*S*)-ethyl lactate or (*S*)-ethyl 3-hydroxybutanoate gave the enol ethers **7a,b** and **8a,b**, and varying the dichlorosilane to dichloromethylvinylsilane gave the enol ethers **9a,b**.

(1) Silicon-Functionalized Silyl Enol Ethers. 2. For 1, see ref 2.
(2) Walkup, R. D. *Tetrahedron Lett.* **1987**, *28*, 511.
(3) Brownbridge, P. *Synthesis* **1983**, 1; 85.
(4) For examples (leading references) of enolate addition reactions featuring stereoselectivity due to a chiral group on the enolate, see: (a) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1. (b) Heathcock, C. H. In *Asymmetric Synthesis*, Vol. 2; Morrison, J. D., Ed.; Academic Press: New York, 1983; Chapter 2. (c) Davies, S. G.; Walker, J. C. *J. Chem. Soc., Chem. Commun.* **1986**, 495. (d) Helmchen, G.; Schmierer, R.; Grotemeier, G., Selim, A. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 207. (e) Nagao, Y., Hagiwara, Y., Kumagai, T., Ochiai, M., Inoue, T., Hashimoto, K., Fujita, E. *J. Org. Chem.* **1986**, *51*, 2391. (f) Braun, M.; Devant, R. *Tetrahedron Lett.* **1984**, *25*, 5031. (g) Masamune, S.; Sato, T.; Kim, B.-M.; Wollmann, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 8279.
(5) Kusnezowa, I. K.; Ruhlmann, K.; Grundemann, I. *J. Organomet. Chem.* **1973**, *47*, 53.
(6) All of the alkoxysilyl enol ethers were synthesized as described in ref 2. Complete spectroscopic data for **4–14** and **16** is given in the supplementary material. Due to the reactive nature of these compounds, samples of a purity adequate for elemental analyses could not be obtained.

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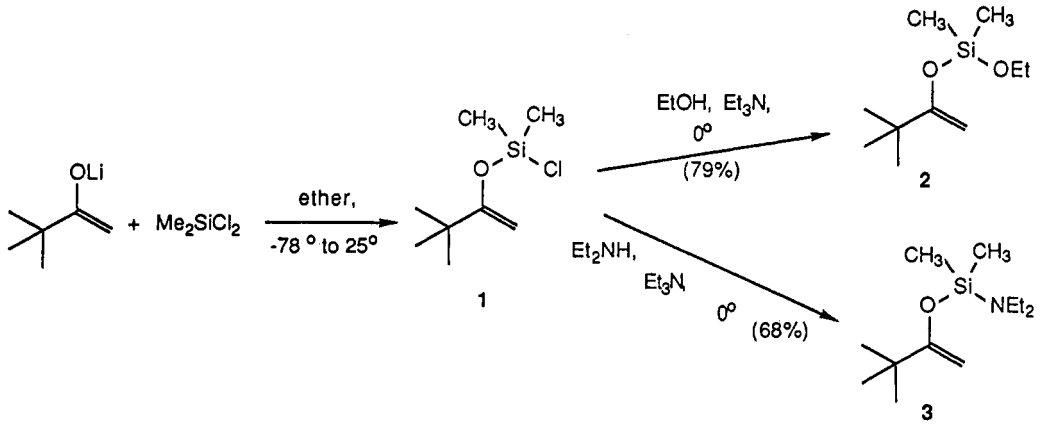
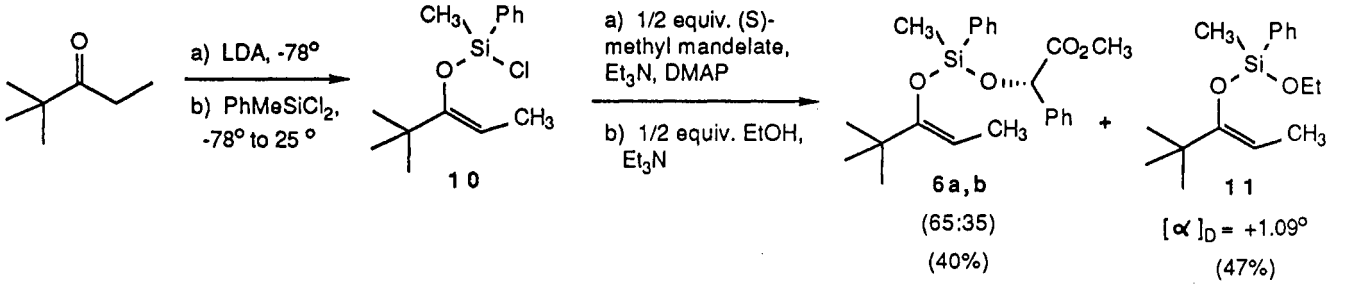
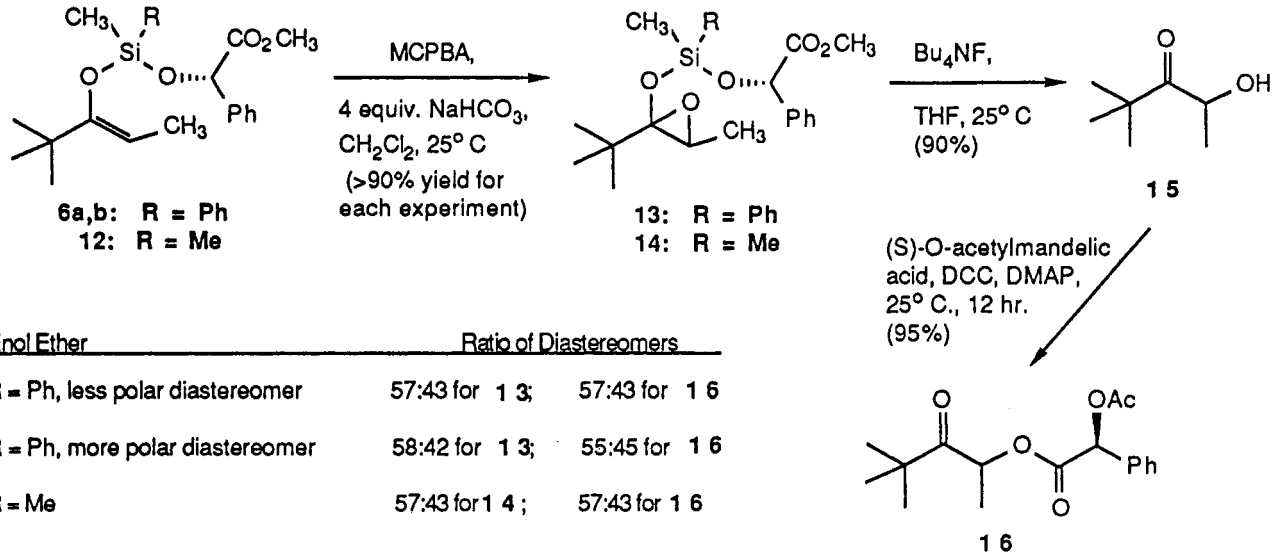
Scheme I



Scheme II



Scheme III



Enol Ether	Ratio of Diastereomers	
R = Ph, less polar diastereomer	57:43 for 13;	57:43 for 16
R = Ph, more polar diastereomer	58:42 for 13;	55:45 for 16
R = Me	57:43 for 14;	57:43 for 16

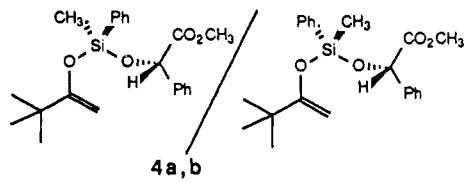
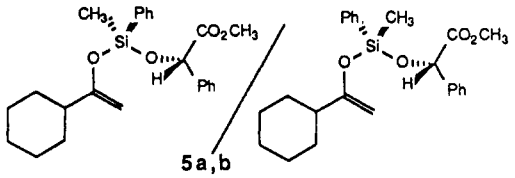
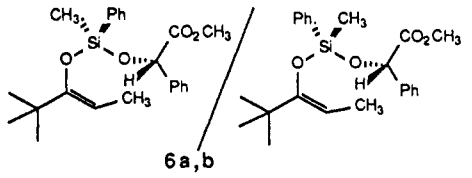
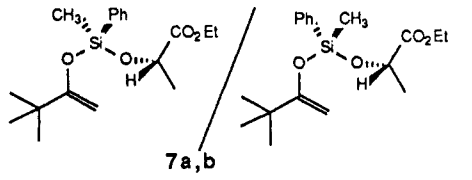
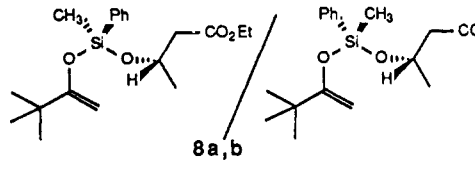
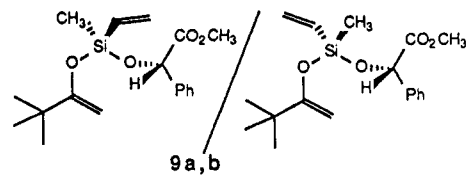
Thus diverse chiral enol ethers can be prepared via chlorosilyl enol ether based methodology.

At this time we cannot assign absolute configurations to the silicon centers in each diastereomer of the enol ethers **4–9**. The NMR data[6] for these compounds suggest that a trend may exist between the structure of a diastereomer and its retentiveness on silica gel. For example, the alkenyloxy group signals are, in general, more shielded in the more polar diastereomer than in the corresponding less polar diastereomer. Such trends, if not just due to coincidence, may be useful for making stereochemical assignments to diastereomeric alkoxysilyl enol ethers. Efforts are being made to assign configurations to these compounds by X-ray crystallography and by chemical correlations with known chiral silanes.[7]

Studies of the synthesis of the enol ether **6a,b** indicated that stereoselective syntheses of chiral silyl enol ethers based on a kinetic resolution are possible. When the racemic chlorosilyl enol ether **10** was formed as indicated in Scheme II and then allowed to react with one-half of a molar equiv of (*S*)-methyl mandelate followed by ethanol, the alkoxysilyl enol ethers **6a,b** and **11**[6] were formed. The ethers **6a,b** formed in this manner were 30% enriched in one diastereomer, and the ethoxysilyl enol ether **11** exhibited optical activity ($[\alpha]_D$ +1.09°, CCl_4 (*c* 0.021 g/mL)).

(7) Reviews: (a) Maryanoff, C. A.; Maryanoff, B. E. In *Asymmetric Synthesis*, Vol. 4; Morrison, J. D., Scott, J. W., Eds.; Academic Press: New York, 1984; Chapter 5. (b) Corriu, R. J. P.; Guerin, C.; Moreau, J. J. E. *Top. Stereochem.* **1984**, *15*, 43.

Table I. Chiral Alkoxysilyl Enol Ethers

enol ether	yield,[a] %	HPLC t_R, min		specific optical Rotations[b]	
		less polar	more polar	less polar	more polar
 **4a,b**	85	11.4[c,d]	13.5	+47.7° (0.0635)	+21.9° (0.0074)
 **5a,b**	30	15.6[c,d]	16.6	+35.7° (0.0044)	+42.4° (0.0055)
 **6a,b**	49	6.4[d,e]	7.0	+42.0° (0.0150)	+24.7° (0.0254)
 **7a,b**	42	12.8[c,f]	13.5	−23.2° (0.0038)	−33.9° (0.0104)
 **8a,b**	44	6.9[e,g]	7.2	+6.4° (0.0104)	+11.5° (0.0218)
 **9a,b**	15	5.9[d,e]	6.2	+37.9° (0.0164)	+43.3° (0.0224)

[a] Yields of the 50:50 mixtures of the two diastereomeric enol ethers obtained following purification by chromatography using 230–400-mesh silica gel and a 90:10 (v/v) hexane:ethyl acetate eluent; 70–80% crude yields of essentially pure enol ethers were obtained in each case, but substantial losses occurred, in some cases, during chromatography. [b] Values represent $[\alpha]_D$ values measured at 25 °C in CCl_4 at the concentrations indicated in parentheses (g per mL solution) on a Perkin-Elmer Model 141 polarimeter. [c] Measured on a Waters Associates Z-Module column with a silica gel cartridge and an eluant of 98:2 (v/v) hexane:ethyl acetate. [d] Eluant flow rate = 1.0 mL/min. [e] Measured on an Advanced Separations Technologies column (25 cm × 4 mm (i.d.)) packed with 10-mm silica gel and an eluent of 98:2 (v/v) hexane:ethyl acetate. [f] Eluent flow rate = 0.5 mL/min. [g] Eluent flow rate = 0.9 mL/min.

The enantiomeric excess of the ether **11** could not be determined by using chiral NMR shift reagents; it was probably similar to the diastereomeric excess found for **6a,b** (i.e. 30% ee). Under optimized conditions, more highly enantioselective syntheses of simple chiral alkoxysilyl enol ethers like **11** may be achieveable.

Few studies of the effects of chiral silicon centers upon the stereochemical outcomes of reactions of organosilanes have been made.[7,8] None of these studies involved silyl enol ethers. We considered the effects of a chiral alkoxy group and a chiral silicon center upon the facial selectivity of the *m*-chloroperbenzoic acid (MCPBA)-mediated epoxidations of enol ethers **6a**, **6b**, and **12**[6] under basic conditions (Scheme III). A modest diastereofacial selectivity (10–14% diastereomeric excess) was observed for the epoxidations of each of the three enol ethers, according to the ^1H NMR spectra of the epoxides **13** and **14**.[6,9–11] The

(8) (a) Daniels, R. G.; Paquette, L. A. *Organometallics* **1982**, *1*, 1449. (b) Hathaway, S. J.; Paquette, L. A. *J. Org. Chem.* **1983**, *48*, 3351. (c) Larson, G. L.; Torres, E. *J. Organomet. Chem.* **1985**, *293*, 19. (d) Larson, G. L.; Torres, E.; McGarvey, G. Abstracts of Papers, 191st National Meeting of the American Chemical Society, New York, NY; American Chemical Society: Washington, DC, 1986; ORGN 203.

(9) Each enol ether gave rise to two diastereomeric (*Z*)-oxiranes. Support for this comes from the observation that *four* diastereomeric epoxides are formed from each enol ether (according to ^1H NMR spectroscopy) when the epoxidation is done under acidic conditions (no added sodium bicarbonate), due to an acid-catalyzed isomerization of the enol ether and/or epoxide.

(10) For another report of a stable silyloxy epoxide, see: Paquette, L. A.; Lin, H.-S.; Gallucci, J. C. *Tetrahedron Lett.* **1987**, *28*, 1363.

(11) The ratios indicated in Scheme III represent averages from triplicate runs of the epoxidation reactions. We estimate that an error of ±2 exists for the reported values of the ratios.

hydroxy ketone 15[12] formed from each epoxide by desilylation was esterified to (*S*)-*O*-acetylmandelic acid[13] to form esters (16) which were analyzed by ^{1}H NMR spectroscopy.[6,14] As indicated in Scheme III, the diastereomeric excesses of 16 derived from each epoxide sample agree with those of the epoxides. In addition, *the major diastereomer of 16 is the same for each experiment.* Therefore, selectivity for epoxidation of the *same* face of the enolate ligand occurred, regardless of the absolute configuration of the silicon atom and irrespective of the existence of chirality on the silicon center. We conclude that the diastereofacial selectivity for the epoxidation of an alkoxysilyl enol ether by MCPBA is affected by a chiral alkoxy group and not by a chiral silicon center.

We considered our choice of the MCPBA epoxidation of silyl enol ethers to be the reaction least likely to exhibit stereoselectivity due to a stereogenic silicon center, because it would involve little, if any, sterically demanding coordination of the reagent to the alkoxysilyl group prior to the addition step. The results described above support this suspicion, but offer the prospect that a chiral alkoxy ligand on the silicon center will by itself offer some degree of a stereodirecting effect. It would be premature to discount the value of a stereogenic silicon center as a stereodirecting element for addition reactions of silyl enol ethers. We are currently investigating the stereochemistry of metal-mediated reactions of chiral alkoxysilyl enol ethers with the idea that metal complexation to the alkoxy ligand may draw the silicon closer to the enol ligand so that the silicon center may exert a significant steric effect upon the approach of reagents to the enol ether.

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Supplementary Material Available: Complete NMR data for compounds 4–14 and 16, IR data for compounds 4–9 (7 pages). Ordering information is given on any current masthead page.

(12) Bowlus, S. B.; Katzenellenbogen, J. A. *J. Org. Chem.* **1974**, *39*, 3309.
(13) Whitesell, J. K., Reynolds, D. *J. Org. Chem.* **1983**, *48*, 3548.
(14) As with the epoxides, replicate experiments yielded the indicated diastereomeric ratios with an accuracy of ±2.

Robert D. Walkup,* Nihal U. Obeyesekere
Department of Chemistry and Biochemistry
Texas Tech University
Lubbock, Texas 79409-4260
Received November 4, 1987

Avermectin Chemistry. 2. A Secure and Flawless Strategy for the Final Synthetic Stages[1,2]

Summary: A cycle of transformations on avermectin B_{1a} shows that problems of conjugation/deconjugation/epimerization during the final stages of synthesis of these systems may be obviated by having an exocyclic methylene at C4. Thus, the labile, biologically important C2 center in such precursors is not affected by oxidations, lactonizations, or rearrangements. Indeed, this location represents a safe place to "park" the Δ^3 bond while gross transformations of the avermectin skeleton are carried out.

Sir: Our recent studies have demonstrated that the final step(s) for a synthetic route to the avermectins (e.g., 1) need to be undertaken with extreme caution.[3] Thus, strategies which employ synthons for the "southern half", such as the "correct" (Δ^3) species I[4,5] or the conjugated (Δ^2) counterpart II[6] are potentially problematic. First, Ia goes readily to II, and deconjugation of II leads not to I, as originally had been claimed,[7a] but to the 2-epi isomer III, exclusively[3,7b] or predominantly,[8] depending on the conditions used (Scheme I). Second, we have observed[9] that oxidation of homoallylic alcohols, such as Ib, leads to substantial amounts of allylic cleavage to give enones, such as IV. *The fact that the C2 stereocenter and the Δ^3 double bond are both crucially important for biological activity[10a] demands a strategy that guarantees, simultaneously, the integrities of both structural entities.* The synthon V should fulfill these requirements, and in this manuscript, we disclose some pertinent results.

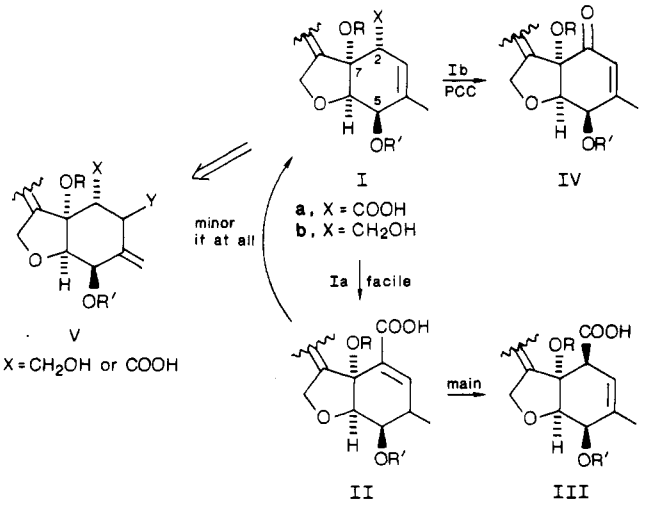
For V, there are two crucial requirements that need to be established: (i) Can macrolactonization be carried out with the exocyclic double bond in place? There is a threat of β-elimination of HY from V (X = "COOH"), which would give a highly conjugated system. (ii) Can the exo → endo rearrangement be carried out *on the macrolactone* without the problematic epimerization/conjugation, of which we had warned?[3]

We decided to test these questions by retrograde and synthetic transformations on avermectin B_1 (**1a**).

The primary alcohol **1b** is known to be the product of selenium dioxide oxidation of **1a**[10] (Scheme II). After some differential protection to give **1c**, the lactone was reduced and the resulting diol was adjusted to give the free allylic alcohol **2**. For endo → exo double bond rearrangement, the chemistry of Nicolaou[11] was utilized to obtain the primary selenide **3**, and Clive's selenoxide rearrangement[12] then gave 4a as a single isomer. Notably, both processes (i.e., **2** → **3** → **4a**) can be carried out in "one pot" in over 90% overall yield.

After appropriate functional group adjustments, the primary alcohol **4b** was oxidized, and the resulting hydroxy

Scheme I



(1) This work was supported by grants from the National Institutes of Health (GM 32569) and Merck, Sharp and Dohme.
(2) Presented, in part, at the International UNESCO Workshop on Natural Products of Potential Medical Value, Tel Aviv, Israel, Dec 15–17, 1986, and at the 4th International Conference on the Chemistry of Biologically Active Natural Products, Budapest, Hungary, Aug 10–14, 1987.

0022-3263/88/1953-0923$01.50/0