THE USE OF METALLOIDS (-SiMe₃, -SnR₃) AS PROTECTED CARBANIONS

SELECTIVE ACTIVATION AND NEW CYCLIZATION PROCESSES

NIELS H. ANDERSEN,* DAVID A. MCCRAE, DOUGLAS B. GROTJAHN, SATISH Y. GABHE, LOUIS J. THEODORE, ROBERT M. IPPOLITO and TARUN K. SARKAR Department of Chemistry, University of Washington, Seattle, WA 98195, U.S.A.

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Abstract—Two aspects of organosilicon and -tin chemistry will be dealt with in this paper: the reactivity of allylmetalloids and the potential of the C-MR₃ function as a protected carbanion which can be unmasked to provide synthetically useful carbon nucleophiles with the primary focus on the latter.

Applications of organosilicon compounds, particularly allylsilanes, to organic synthesis gained prominence starting in the mid-1970's, largely through the work of Hosomi and Sakurai, Fleming, and Calas. This area has been the subject of two excellent reviews and experimental details are available;¹ thus an account here is unnecessary. It should be noted however that besides Wittig olefination procedures² and a few Diels-Alder pathways, allylsilanes have been prepared either from more reactive allylmetal systems or via reductive silylation, of which the pinene based chemistry of the Calas group is representative (Scheme 1).³

It should also be noted that allylsilanes serving as carbon nucleophiles, eqn (1) (MR_3 =SiMe_3) is by no means a universally applicable principle. Carbonyl compounds (and their acetals), whether conjugated or not, are generally excellent electrophilic partners in this reaction, but alkylations have only rarely been observed. Epoxides

$$\begin{array}{c} R_{3}M \\ R_{x} \\ R_{x} \end{array} + e^{+} - R_{x} \\ R_{x} \end{array}$$
eqn (1)

^aHosomi et al.⁷ report that allyltrimethylstannane reacts in a comparable manner to the silane with aldehydes, ketones, enones, and acetals. Prenyl(3-methyl-2-butenyl)trimethyltin was the only unsymmetrical allyl system examined; it did react with allylic transposition. As noted, increased π -bond nucleophilicity would be expected as a correlate with the lower ionization potential displayed by allylstannanes.

have not figured in such alkylations. Finally, as noted by Magnus,⁴ if allylsilane chemistry is to find a useful place in organic synthesis, truly versatile methods for introducing the Me₃Si-C unit into complex functionalized molecules must be found.

Allylstannanes can, a priori, be viewed as a more nucleophilic version of the silicon compounds." Only in the last couple of years has there been any significant application of allyltin chemistry in synthesis even though the addition reaction with carbonyl compounds surfaced in the organic literature long before those of the lighter metalloids. In 1967 König and Neuman reported⁵ both the thermal and ZnCl₂ catalyzed version of this reaction. These applications can be divided into two classes: those which are clearly radical in character⁶ [catalyzed by AIBN, thermal or light induced, and very likely those processes catalyzed by Rh (I). Pd (O), and Pd (I) complexes]; and those which are conceptualized as heterolytic or concerted [thermal reactions with carbonyls?, and reactions catalyzed by protic or Lewis acid and by nucleophiles]. Only the latter will be considered.

A few scattered applications of allylstannanes appeared through the seventies,⁸ including notable cases of selective allylation of quinones.⁹ Recent studies of the chemo-¹⁰ and stereo-selectivity¹¹ of allyltin addition ot carbonyls suggest a bright future in synthesis. However there is some evidence for 1,3-tin migration^{6a,8a,12} and the allylic transposition regiochemistry of eqn (1) has not been universally observed even in Lewis acid catalyzed reactions. In one case the stereoselectivity is not altered



by the double bond configuration: Yamamoto et al.^{11b} report:



In another case, in which the allyltin species are generated in situ, threo-products are reported from the trans species:¹³

Metalloids as sources of reactive carbanions. The use of vinyltin species for the generation of vinyllithiums is well known; Piers' generation of a β -acylvinyl anion equivalent serves as a recent example.¹⁹ The alkyllithium induced

$$\frac{1}{2}C-SnR_3 + RLi \longrightarrow \begin{bmatrix} 2C-SnR_4 \\ Li^+ \end{bmatrix}$$

∋ເ⊇r+

transmetallation (presumably via the "ate complex", has also been used to generate allyl-lithiums,^{20a} 1,3-dithian-2yllithiums,^{20b} and α -alkoxyllithiums^{20c} as well. The fluoride-induced cleavage of C-Si bonds is the basis for



The greater reactivity of allyltin species may also allow for allylation of epoxides¹⁴ and other less reactive electrophiles.

An additional potential advantage of allyltin species is the availability of other methods for the allylic introduction of SnR₃. The Diels-Alder, Wittig,¹⁵ and alkylative (R₃SnCl) methods suitable for SiR₃ apply here; but the superior nucleophilicity of R₃SnLi^b offers approaches not available for allylsilanes. Syntheses of allyltin (and -silicon) species are available via alkenylboronates^{11a} but only the tin species can be prepared from a wide variety of allyl-X units:



selective removal of several new protecting groups;²¹ however it had not figured in synthesis as the source of nucleophilic carbon until 1978.^c

Our entry into the allylmetalloid area stems from an interest in the ene cyclization (intramolecular Prins reaction) of olefinic aldehydes.²³



As anticipated the substitution of $X=SiMe_3$ for X=H did facilitate the reaction²⁴ and produced the exocyclic olefin isomers as sole products even in cases that had previously (X=H) afforded significant quantities of endocyclic olefin products. The closure to 5-membered rings was a general reaction only when $X=SiMe_3$.

 ${}^{b}R_{3}SnLi$ species react with a wide variety of alkylating and allylating agents,¹⁶ including tosylates¹⁶⁰ and epoxides^{16c}; with secondary halides with S_N2 inversion^{16c} is observed. W. C. Still has put this reactivity to use in a number of protection strategies not directly related to the present work.

^cFluoride induced C-Si cleavages have been used to generate reactive neutral species such as: cycloheptatrienylidene,^{22a} oand p-quinodimethanes,^{22b} and a xylylene intermediate for steroid synthesis.^{22c} In the latter case KF/diglyme at ambient was employed, but it is unclear to what extent the reaction was governed by F^- or electrophilic epoxide opening.





Aldehyde 5, for example, which unlike aldehyde 4 does not cyclize to completion with 0.1 equivalent of SnCl₄ at -35° , cyclizes rapidly at -78° with a stoichiometric amount of SnCl₄ in CH₂Cl₂.^d The initial products are silyl ethers 7 and 9 (59:41) which undergo hydrolysis on quenching with saturated aqueous NH₄Cl.^e

With $BF_3 \cdot Et_2O/CH_2Cl_2$ (-78° or 0°, 15 min), aldehyde 5 affords alcohols 6 and 8 (85:15 ratio) independent of the quench employed.^e To determine whether the increased stereo-selectivity reflected a change in mechanism to a nBu_4NF catalyzed reactions of allyltrimethylsilane and a variety of aldehydes. Aldehyde 5 reacts at a practical rate even at room temperature. Some degree of participation (eqn 2) may improve the intramolecular case.

This result prompted us to explore other instances in which a C-SiMe₃ unit would serve as a source of a nucleophilic carbanion. We examined the generation of the 1,3-dithian-2-yl anion since its conjugate acid is of comparable pK_n to propene.¹ Our initial results are collected below:



fluoride promoted cyclization (eqn 2), we have examined the reaction of aldehyde 5 with Bu₄NF in anhydrous THF. After a 1.5-h exposure to 3 equivalents of the fluoride at 50°, only alcohols 6 and 8 could be detected. The equatorial isomer (8) constitutes 82% of the volatile product. The "push" and "pull" mechanisms display diametrically opposed stereoselectivities. Fluoride ion induced production of a nBu_4N^{\oplus} allyl-carbanion appears facile even relative to the intermolecular analogies that appeared at about the same time. Hosomi *et al.* reported²⁵ reaction times of 4-48 hr (at 66°) for the

¹The acidity of the 2-position hydrogens on 1,3-dithiane has been measured as: $pK_a = 31.1(Cs^+ \text{ counterion}, \text{ cyclohexyl-amine}),^{26} \approx 35$ (Li⁺, THF-HMPTA);²⁸ and estimated as ≈ 38 (K⁺, DMSO).²⁷ In THF without added HMPTA 1,3-dithian-2-yllithium is an aggregate, the resulting increase in conjugate base stability produces an apparent $pK_a \approx 31.^{28}$

⁶The partitioning between protodesilylation and methylation was not shifted significant toward protodesilylation by the use of a 10-fold excess of nBu₄NF reagent solutions. Independent of the electrophile employed, protodesilylation (yielding 12) competed with the desired substitution reaction. In retrospect, it is clear that some portion of the protodesilylation was associated with adventitious water in our nBu₄NF reagent solutions, but this was not a full explanation for the results.[#]

We were unable to obtain allylsilane-like behavior toward activated electrophiles with silane 10: additions to aldehydes, acetals, and enones could not be effected under Lewis acid (SnCL, TiCL, BBr₃, BF₃·OEt₂, or MgBr₂) catalysis.

A selection of results obtained for silyldithiane 10 and a variety of electrophilic reagents using nBu₄NF solutions of reproducible activity^h appear in Table 1. A worst case analysis of the data allows less than 0.2 equiv F^{\odot} in our reagent solutions (*vide infra*). When dithiane 10 reacts in the absence of an electrophile, protodesilylation occurs rapidly ($t_{1/2} \ll 1$ min at 22°, < 15 min at -10°) with concomitant production of tri-n-butylamine indicating that β -elimination is serving as a proton source. We view this as the result of collapse of an intermediate contact ion pair (11) which forms rapidly at temperatures of about -20°.

When D_2O is present as an electrophile, varying amounts of deuterium incorporation are observed in the product dithiane (entries 2-5). β -elimination of tributylamine competes quite effectively as a quench for ion pair

^d Aldehyde 4 does not react in the presence of SnCL until a temperature of -40° is reached.

^{&#}x27;In order to detect the silyl ether intermediates in the SnClcatalyzed process, the reaction must be quenched by addition of Et₃N prior to adding aq. NH₄Cl. Silyl ether hydrolysis occurs only when the ethers are present as the Lewis acid complexes on aqueous quenching. BF₃·Et₂O/CH₂Cl₂ hydrolyzes silyl ethers 7 and 9 independent of the quench employed.

Table 1. Tetrabutylammonium fluoride^h induced reactions of 2-trimethylsilyl-1,3-dithiane

electrophilea)	_F eb)	reaction conditions	nBu ₃ Nc)	product	ratio 13-16:12d)
1 none	1.0	22°, 12 min	1	12	
2 D ₂ O 3 D ₂ O 4 D ₂ O 5 D ₂ O	1.0 1.0 5.0 1.0	-20°, 12 hr; 22°, 1 hr -10+22°, 6 hr -10°, 45 min -10°, 10 ming)	~~~~	13a 13a 13a 13a 13a	73:27 e.f) 63:37f) 43:57f) 62:38f)
	1.0 1.0 1.1 1.1j) 1.0k) 10 1.0 0.1 1.0 0.1	-60°, 1 hr 22°, 30 min 22°, 20 min -15°, 60 min 0°, 8 min -5°, 15 min -10°, 15 min 0°, 30 min -10°, 20 min	√ n.d. n.d. n.d. trace trace n.d. trace	13b 13b 13c 13c 13c 13c 13c 13c 13c 13c 13c 14a+b 84% 14bh) 70% 14c ¹) 15a	33:67 31:69 26:74 38:62 13:87 11:89 94:6 >97:3 >96:4
15 nC ₇ H ₁₅ CHO (2 eq.)	1.0	0°, 30 min	trace	<u>156</u>	-20:80
16 $C_6H_5COCH_3$ 17 $C_6H_5COCH_3$ 18 $5-C_6H_5-cyclohexenone$ 19 $5-C_6H_5-cyclohexenone$	0.1 0.1 0.1 0.1	-60+22°, 3 hr -60+20°, 71 hr -10°, 15 min -60°, 9 hr	trace trace trace trace	<u>16a</u> 16a 16b	<5:95 =4:96 <4:96 ≷4:96 ≷4:96

a) Five equivalents of electrophile unless otherwise indicated; b) molar equivalents (per mole 10) of nBu4NF employed; c) a check indicates 20^{+} % nBu3N observed by gc, trace implies <5%; d) amount of 12 determined by quantitative gc except in entries 2+5, product identity and ratio confirmed by NMR throughout; e) confirmed by GC/MS; f) ratio from NMR integral and C-2 hydrogen peak shape and multiplicity agree ±5%; g) reaction carried to 25% completion; h) isolated yield of pure silyl ether 14b; i) isolated yield alcohol 14c, presumably silyl ether hydrolysis is completed upon chromatography; j) nBu4NF was added dropwise over the reaction period; k) identical results by direct or inverse addition.



11. The decrease in deuterium incorporation with increasing temperature or increasing amount of ammonium cation is in accord with this hypothesis. Our generous estimate of maximal water content is based on this increase assuming that H_2O is the sole source of added protium in the product.ⁱ Reactive alkylating agents appear to be comparable to water as competitors against ion pair collapse.

Non-enolizable aromatic aldehydes give adducts (14, 15a) in excellent yields with little dithiane formation.

Less reactive aliphatic aldehydes (e.g. entry 14) give only modest adduct formation. Only traces of product could be detected with acetophenone. In all cases involving enolizable carbonyl compounds, nBu₃N is formed in reduced amounts. The nBu₃N:12 ratio is less than one quarter the value observed in entry 1 or during alkylation attempts, suggesting that α -proton abstraction competes with β -elimination.

In order to allow intermolecular reaction of the naked dithiane anion with electrophilic centers less reactive than aromatic aldehydes it will be necessary to have a counterion that has no extractable protons. Our efforts to achieve this using alkali fluorides [KF or NaF, 18-crown-6, THR, 0-40°; CsF in tetraglyme or $(EtOCH_2CH_2)_2O$ at 0-80°] have not been particularly successful. Alkylations (MeI, nBuI) could be effected only in low yields, 0-7%. With our best electrophile, piperonal, stirring with excess KF (20 mole % 18-crown-6) required 2 days at ambient to

^{*}Indicated as TBAF^{*}, at see Illustrative Experimental Procedures.

^{&#}x27;That post-quench exchange is not responsible for deuterium incorporation was demonstrated by stirring dithiane (1 equiv), D_2O (5 equiv) and nBu_4NF (1 equiv) at 22° for 6 hr. No deuterium incorporation was observed ($\leq 5\%$).

achieve practical yields (>70%) and the product (14a) was not as clean as that obtained using nBu₄NF.

Hosomi et al.²⁵ noted that KF-crown was ineffective for allylsilane aldehyde reactions. Lipshutz and Pegram have concluded that adventitious H₂O is the source of the unique facility of nBu₄NF for cleavage of the β trimethylsilylethoxymethyl group^{21b}—other R₄NF and KF—crown are not effective. What will be required is a tetraalkylammonium ion lacking β -hydrogen but having solubilizing characteristics similar to nBu₄N^{\oplus}. Efforts directed toward this goal are in progress.

Cyclization reactions based on 2-trimethyl-1,3-dithiane. Even though our efforts to effect fluoride induced intermolecular reactions of 2-silyldithiane were limited practically to aromatic aldehydes, our previous work with the ring closure using allylsilanes prompted us to examine an intramolecular version of the reaction of 2-silyldithiane and carbonyl compounds.

The use of dithianyllithium reagents for cycloalkylation (eqn 3) is an established technique²⁹ and has also been explored using alkyllithium cleavage of a 2-stannyl group: However the corresponding cycloaddition $(17 \rightarrow 18)$ has not been realized by transmetallation. The fluoride C-Si cleavage alternative works surprisingly well,³⁰ in light of the poor yield observed for its intermolecular equivalent. The syntheses of the requisite aldehydes (19a-e) are collected in Scheme 2.

The lithic derivative of 10 could be alkylated in uniformly high yield even with bromoacetaldyhyde acetal $(\rightarrow 22a)$. Two other features warrant mention: (1) the successful PCC oxidation in the presence of a silyldithiane unit, and (2) the efficient acetal hydrolysis sequence involving the accelerated aqueous hydrolysis of the stoichiometrically formed SnCL complexes. This sequence, brief treatment with SnCL at Dry Ice temperature followed by an aqueous quench, has proven to be generally applicable to acetals.

With the exception of aldehyde 19a, all of these cyclization substrates underwent rapid formation of the spiroalcohols (18) upon treatment with nBu₄NF at room temperature. The yield exceeds that of the intermolecular octanal reaction in each case. Only in the case of 7-membered ring formation did protodesilylation



Reagents: *i*, 1.1-1.5 equiv. BH3·THF, 2-4 hr, 25°; *ii*, pyridinium chlorochromate, CH₂Cl₂, 2-3 hr, 25°; *iii*, (MeO)₃CH, MeOH, Amberlyst-15, \mathfrak{B} 3-12 hr, 25°; *iv*, HBr. MeOH, CH₂Cl₂; *v*, 2-trimethylsilyl-1,3-dithian-2-yllithium in THF, -78-0°C over a 1 day period; *vi*, 1.1 equiv. of SnCl4 or TiCl4, -78°, 1 hr, then aq. NH4Cl quench.

Scheme 2. Synthesis of 2-(ω -oxoalkyl)-2-trimethylsilyl-1,3-dithianes. Throughout homologs are indicated by: a, n = 1; b, n = 2; c, n = 3, d, n = 4; e, n = 5.



compete with cyclization and an intermolecular component. We have not yet assessed the extent to which the acidic methylene protons α to the carbonyl were responsible for the competing protonation in this case, eqn (5). The 2-protiodithianylaldehyde (17e) was isolated in 10-15% yield.

The cyclization reaction can also be accomplished in a catalytic cycle. Upon treatment with 0.1 equiv of nBu₄NF/THF, silylaldehyde 19d cyclizes in



Thus, even though the nBu_4N^{\oplus} counterion has obvious deficiencies which will presumably be overcome when a new generation of tailored fluoride sources become available, TBAF does provide a means of effecting cyclization reactions' which would be impossible under typical transmetallation conditions for generating dithiane anions.



greater than 70% yield in 2 hr at 22°. The silylether (24) is the major product under these conditions.

Alkyl-substituted dithianylmetal derivatives usually do not serve for Michael additions to enones. However we have demonstrated this process in the intramolecular system using the *in situ* generated tetrabutylammonium derivatives. The silylaldehydes undergo the Emmons' condensation to enones (25, 26) under the standard conditions.³¹ 5-Membered Comparative studies of trimethylsilyl and trialkylstannyl cleavage reactions. The potential of fluoride induced C-SiMe₃ cleavage as a source of carbon nucleophiles has been demonstrated in the previous sections. Low temperature alkyllithium induced C-SnR₃ cleavage has been shown by others and it is clear that the C-SnR₃ cleavage can be carried out in the presence of C-SiMe₃ units without complications. We were therefore interested in examining stannanes under conditions designed to cleave



ring formation $[25c \rightarrow 27(n = 3)]$ occurs readily (64% isolated yield) using 1.1 equiv of nBu₄NF at ambient. 6-Membered ring formation appears more difficult (yields 20-40%) and the use of catalytic quantities of nBu₄NF the C-Si bond to see if complete selectivity could be expected in polyfunctional cases. Also, since alkyllithiums, even at $-110--60^\circ$, are not compatible with many functional groups in common synthetic use, we wished to explore milder methods for carbanion generation from stannanes. It is known the allylstannanes undergo alkali and alkoxide induced demetallation at rates from two to three orders of magnitude greater than those of the corresponding silicon systems.³² We there-

⁷The intramolecular nature of the reactions were established by the GC characteristic of the products (18b \rightarrow e; 25c, d) and PCC oxidation of 18b \rightarrow e to dithiaspiroalkanones (characteristic ν C=O).

The use of metalloids (-SiMe₃, -SnR₃) as protected carbanions



fore examined silane 10 and the corresponding tin compound, (1,3-dithian-2-yl)trimethylstannane (29) with a variety of basic and nucleophilic catalysts including KFcrown and nBu₄NF. Stannyldithiane 29 proved very sturdy in the presence of fluoride ion and on this basis one can anticipate selective reactive cleavage of silyl functions in the presence of C-Sn bonds.

Even aromatic aldehydes gave at best a 5% yield of addition products after 6 days at ambient. Protodestannylation was also a slow reaction, typically the half life for stannyl dithiane disappearance was ca. 6 days at 22°. The only reaction which proceeded to any significant extent was allylation. The absence of a comparable reactivity toward methyliodide prompts us to suggest alternative mechanisms in this case eqn. (6).

The [2,3]-sigmatropic rearrangement has previously been noted in the dithianylids.³³ After 3 days at 40°, 2-allyl-1,3-dithiane was isolated in 45% yield together with a 30% yield of the protodestannylation product. Metalloid substituted dithianes may represent an access to dithianylids which avoids the use of highly basic media.

In 0.1 M MeONa/MeOH dithianes 10 and 29 both undergo protodemetallation. The rates of reaction were however entirely contrary to expectations,^k $t_{1/2}$ at 22°: 6 hr for silane 10, ~48 hr for stannane 29. In the absence of a proton source LiOMe was ineffectual as a catalyst for condensation reactions between 10 (or 29) and a variety of esters (RCO₂Me) or aromatic aldehydes. In the case of silane 10 alkoxide catalysis has been attempted in THF, tetraglyme, DMSO, and THF-HMPTA without notable reaction. In the absence of excess ROH no desilylation was observed even after 2 days at ambient.

However the previously recorded nBu_nNF catalyzed additions were shown to be mediated by fluoride throughout, not by alkoxide in the following way: In the case of MR_3 =SiMe₃, even though no reaction was observed over 2 hr at -10° , a rapid conversion took place upon addition of a catalytic amount of fluoride to the cooled reaction mixture.

We are currently examining a variety of nucleophiles as potentially selective activators of C-SnMe₃ via "ate" complex formation.

Metalloid and counterion control of regiochemistry. The lithio derivatives (30) of ketene dithioacetal or alkenyldithianes (31) are known to react with α -selectivity with most hard electrophiles.^{35,36} Aromatic aldehydes and ketones however give nearly exclusive y-addition with derivative 30a²⁹ and for the cyclohexenyl derived system we have been unable to direct alkylations or aliphatic aldehyde additions to the γ -position. Although Ziegler's cuprate method³⁷ may provide a partial solution for promoting γ -regiochemistry in 30a, it appeared that all vlmetalloid chemistry would offer some attractive possibilities. This impression was immediately strengthened when we carried out reactions of 30a and 30b with R_3MCl . The cyclohexenyldithiane system afforded the α -metallo derivatives (32b, 33b), however 30a gave regiospecifically distince reactions: stannylation afforded only the γ product (35).

The allylsilanes (32a, b, and c) gave the anticipated protodesilylation with transposition on acid treatment or chromatography on silicic acid: ketene dithioacetals (e.g. $32a \rightarrow 34$) were obtained. Careful chromatography on neutral silica or alumina however could be used to obtain the pure α -silyl derivatives. Stannane 35 was less stable, surviving a rapid chromatographic filtration which yields material suitable for further reactions, but undergoing destannylation with allylic transposition affording the thermodynamically disfavored 2-vinyl-1,3-dithiane (31a), to the virtual exclusion of its stable isomer (34). This however proved to be the last instance of typical allyl-



^kThe cleavage of the silane (10) was expected based on a previous literature account;³⁴ however we had expected the stannane to be *more* reactive.³²

Rß

<u>30a</u> b c metalloid behavior encountered in our studies. In numerous trials we were unable to effect Lewis acid (SnCl₄, BF₃·OEt₂, BBr₃, TiCl₄, AlCl₃, ZnI₂, ZnCl₂)





promoted reaction of 32a, 32b, 33b, or 35 and a variety of electrophiles: ClCH₂OCH₃, allyl bromide, anisaldehyde, BrCH₂CO₂Et, BrCH₂CH₂CH₂CH(OMe)₂, ClCH₂CH(OEt)₂, acrolein, piperonal,⁴ and CH₂=CHCH(-OCH₂CH₂O-).^m It would appear that the thioether linkages produce a significant alteration in the reactivity of allylmetalloids. In the course of these studies one unusual redox reaction was uncovered. Stannic chloride converts silane 32b to the known ³⁵ oxidation product (36), presumably with the formation of SnCl₂. This transformation was observed in

¹Piperonal in the presence of $BF_3 \cdot OEt_2$ did produce the α adduct (40c) in low yield from stannane 35. This may reflect a minor fluoride catalyzed component (vide infra) in this reaction.

^mWe did not attempt all possible combinations listed, but each allylmetalloid was reacted with at least one alkylating agent and one carbonyl compound under a variety of conditions. several instances, particularly during attempted alkylation with BrCH₂CO₂Et.

The studies with the cyclohexenyl systems were conducted in 1978, prior to our work on the definitive studies of 2-trimethylsilyl-1,3-dithiane and our only goal at that time was a process that would give γ -addition; numerous cases of modest success at introducing functionality at the α center were not pursued. Among these, two warrant some mention. Ethylene oxide in the presence of SnCL gave the α adduct. In one case methoxymethylation was observed in the presence of TIF.

A more detailed examination of the fluoride induced reactions has been carried out only in the case of 32a and 35.

Silane 32a reacts rapidly with nBu₄NF/THF producing the vinyldithiane in analogy to the α -protonation of 30a. In the absence of added water or other electrophiles minor amounts (5-30%) of ketene dithioacetal 34 are also obtained, presumably the result of subsequent base catalyzed equilibration. In the presence of H₂O (D₂O) or other electrophiles the proportion of 34 decreases. In the presence of 10 equiv of CH₃I, a 74:24 mixture of 31a and 40b is obtained after 15 min at ambient. The stannyl system (35) is also cleaved under comparable conditions. Exact rate comparisons have not been performed to date, but it is clear that the allylstannane (35) is much more reactive than the stannyldithiane (29). This may be a reflection of more facile formation of the "ate" complex (38). Alternatively "ate" complex formation may occur with both 29 and 35 but only in the latter case does the reaction proceed: due to either the enhanced reactivity of the allyl stannate or to facilitated collapse to the ammonium carbanion (37).

Both vinyldithiane derived allylmetalloids react with piperonal at temperatures as low as -20° in the presence of stoichiometric TBAF in minutes. Only modest competitive protodemetallation (5-10%) was observed, the α -(40c) and γ -adducts (39) were isolated in a 3.5:1 ratio upon chromatography of the product mixture. We have confirmed that piperonal (like other aromatic aldehydes^{29,35}) affords a ca. 9:1 mixture of adducts favoring the γ product when the reaction is carried out using the lithio derivative (30a). It is tempting to ascribe this regiochemical change to the intervention of a naked allyl anion (37) in both cases. The α : γ ratio was confirmed in an NMR experiment: a mixture of allylsilane 32a and piperonal in CDCl₃ is converted (ca. 20%) to the previously observed products $(\alpha: \gamma \ge 3:1)$ during the first 30 sec at ambient.

Preliminary trials with allylstannanes that do not bear thioether substituents demonstrate that TBAF catalyzed reactions with carbonyl compounds are a general feature of this class, not a peculiarity associated with the dithiane moiety. An exploration of the regiochemical control potential of allylmetalloids with these varying activation schemes is now in progress.

ILLUSTRATIVE EXPERIMENTAL PROCEDURES

All solvents were anhydrous, glass-distilled; THF was distilled continuously from Na/benzophenone ketyl. All reactions were performed in serum stoppered flasks under an argon atmosphere. TBAF was prepared by titrating nBu₄NOH with aqueous HF. Water was removed by repeated benzene azeotroping on a rotary evaporator until crystalline TBAF was obtained. The resulting material was again benzene azeotroped, and the free flowing crystals were dried in a vacuum desiccator. A THF solution (0.08-1.0 M) was prepared every few days. TBAF solutions indicated by TBAF¹ are prepared by weighing TBAF into a dry flask charged with freshly activated 4A Molecular Sieves. The requisite volume of freshly distilled THF is added. The resulting solution is used during the period 1-8 days after preparation.

Synthesis and cyclization of silylaldehyde 5. Photocitrol^{23b} (6.5 mmole) was bis-silylated by adding a THF soln (7 ml) of the alcohol to a hexane soln (30 ml) containing 35 mmole BuLi and 40 mmole TMEDA. After 5 h the resulting soln was cooled to 0° and 5.6 g (47.5 mmole) of Me₃SiCl was added dropwise. After 30 min, 60 ml of 10% NH₄Cl/aq was added; ethereal extraction afforded an oil which was refluxed in 150 ml MeOH for 12 hr.

Trans, syn-2-(3'-trimethylsilylisopropenyl)-5-methyl-cyclopentyl carbinol (54% yield) was isolated after SiO₂ chromatography of the concentrate: bp 100° (bath, 0.2 torr); ν 1640, 1260, 850 cm ¹ (CH₂=CCH₂SiMe₃); δ (CCl₄) 0.03 (9H, s, SiMe₃), 0.9 (3H, d, Me),

1.51 (2H, s, CH₂Si), 3.52 (2H, d, 6 Hz; CH₂OH), 4.52 and 4.71 ppm (2H, s; C=CH₂); m/e found 226.1740 (C₁₃H₂₆OSi-1.0 mmass).

The alcohol was tosylated (1.2 equiv TosCl/pyr, 14 hr, 22°, 89%), and the resulting tosylate (2.26 mmole) subjected to NaCN (1.1 equiv) in 10 ml of HMPTA at 24° for 16 hr.Chromatographic (SiO₂, C₆H₆) purification and distillation (0.5 torr, 120° bath) afforded the nitrile (63% yield): ν 2280, 1645, 870, 1270 cm⁻¹; δ (CCl₄) 1.45 (2H, s., CH₂Si), 2.18 (2H, CH₂CN); *m/e* 235.1754 (C₁₄H₂₅NSi + 0.2 mmass). A 1.48 mmole portion of the nitrile in 9 ml Et₂O at 0° is converted to 5 by treatment with 2.6 mmole of iBu₂AlH for 2 hr. The resulting reaction mixture was rapidly forced through a 15-g column of SiO₂, which is subsequently washed with C₆H₆ affording an aldehyde sample (80–90% yield) suitable for further reactions.

Product ratios (6-9) for cyclization experiments were determined by GC (150°, 24' Carbowax 20 M). Authentic samples of 6 and 8 were available from previous studies; 23a,38 the corresponding silyl ethers (7,9) were prepared by Me₃SiCl/pyr treatment. Lewis acid catalyzed cyclizations were performed by adding the stated amount of catalyst (as a 0.1 M soln in CH₂Cl₂ or C₆H₆) to a precooled soln of aldehyde (10-30 mg/ml). After the specified time the reaction was quenched by addition of 4 equiv of Et₃N followed by aq. NH₄Cl. With 1.0 equiv SnCl₄ at -35° (10 min) the gc product ratio was: 47% 7," 49.7% 9, 1.5% 6, and 1.7% 8. On a preparative scale: to 430 mg 5 in 15 ml CH₂Cl₂ at 0° there was added 110 mg SnCl₄ in 10 ml CH₂Cl₂. After 10 min the reaction was poured into 100 ml sat aq NH₄Cl. The crude product was chromatographed (2.5% EtOAc/C6H6 on SiO2) affording (after rechromatography of a mixed fraction): 125 mg (42%) of 6, m.p. $64-66^{\circ}$, ^{23*a*} and 113 mg (38%) of alcohol 8—as an oil homogeneous by GC³⁸—*m*/*e* 166.1364 (C₁₁H₁₈O + 0.6 mmass).

The cyclization of 15 mg 5 in 1 ml THF at 50° was initiated by the addition of 3 equiv TBAF (as a 0.88 M soln). GC revealed complete reaction with a 18:82 ratio 6:8 after 1.5 hr. GC indicated that protodesilylation (\rightarrow 4) accounted for <4% of the material.

General procedure, TBAF⁴ catalyzed or induced reaction of dithianes 10, 29, and 32a. A 10 ml flask equipped with a magnetic stir bar was flamed dry, cooled under argon, and charged with dithiane (1 mmole), electrophile (5 mmoles), and dry THF (4 ml). The stirred soln was cooled to the desired temp. and treated dropwise with the desired amount of TBAF⁴ (as 1 M soln in THF). The reaction was monitored by withdrawing 25 or 50 μ 1 aliquots which are quenched with water, partitioned between water and hexane (400 μ) and injected into the GC. When all starting material was consumed, the reaction was poured into 15 ml H₂O, extracted with CH₂Cl₂ (3 × 25 ml), washed with brine, dried over Na₂SO₄, and rotovapped to remove solvent.

All starting materials and most of the products could be assayed quantitatively under a single GC condition— $6' \times 0.125''$ UCW 98 at 175°, N₂ carrier, FID—the relative retention values observed were: piperonal, RR = 1.00: nBu₃N, 0.54; aceto-phenone, 0.26; octanal, 0.17; dithianes 10, 1.08; 12, 0.39; 13b, 0.96; 13c, 0.37 (unresolved from 12, DEGS column employed); 29, 2.11; 31a, 0.67; 32a, 1.74; 34, 0.80; and 35, (not suitable for assay). The results in Table 1, and elsewhere in the discussion are based on these GC assays with tlc and NMR confirmation.

Synthesis of silyl ether 14b (from dithiane 10). The procedure was followed using piperonal (5.0 mmoles, 750 mg) as electrophile and TBAF⁴ (100 μ l of 1 M soln). GC analysis indicated complete reaction within 15 min. The reaction was worked up as described to obtain a clear oil which was chromatographed on 30 gm of MN silica gel eluting with 10% EtOAc/hexane. A clear oil (282 mg, 84%) was obtained which crystallized on standing in a freezer: m.p. 67-70°; δ (CDCl₃) 0.10 (9H, s; OTMS), 1.58-2.28 (2H, m; H-5), 2.75-3.0 (4H, m; H-4, 6), 4.23 (1H, d, 7; H-2), 4.70 (1H, d, 7 Hz; CHOTMS), 5.98 (2H, s; O₂CH₂), 6.82 (1H, s; H-2'), and 6.90 ppm (2H, AB; H-5', 6').

Synthesis of 2-(5'-oxopentyl)-2-trimethylsilyl-1,3-dithiane (19d) and its cyclization. Bromoacetal 20d was prepared (74% yield) from the previously available³⁹ aldehyde [9.7 mmole in 25 ml MeOH containing 0.28g Amberlyst-15[®] and 2.0 ml HC(OMe)₃; 12 hr, 22°]. Dithiane 10 (6.32 mmole) in 30 ml THF was lithiated with 6.4 mmole nBuLi/hexane initially at -78° , then at -20° for

[&]quot;The axial silyloxy compound (7) is underestimated by GC due to minor decomposition on injection.

3 hr. Bromoacetal 20d (6.9 mmole) was added; after 2.5 d at 22°, aqueous work-up and chromatography (SiO2/hexane) afforded 1.65 g (80%) of 22d: δ 0.20 (9H, s; SiMe₃), 3.27 (5.4H, s; OMe), 4.19 ppm (0.85H, m; -CHO₂). The general procedure for acetal hydrolysis $(22 \rightarrow 19)$ follows: 2 mmole 22 in 50 ml CH₂Cl₂ is cooled to Dry Ice bath temperature with stirring and 2.2 mmole neat SnCl4 (or TiCl4, MgBr2 OEt2) is added by syringe. After 1 hr of stirring and cooling the mixture is dumped into 100 ml of sat'd NH4Claq with vigorous shaking. The resulting CH2Cl2 layer affords 19 in 88-96+% yield. In the case of 22d, there was obtained 19d (96%): $R_f = 0.35$ (CH₂Cl₂/SiO₂); δ 0.15 (9H, s; SiMe₃), 1.1-1.8 (5.5H, m), 1.8-2.4 (5.5H), 2.4-3.4 (5.3H; dithiane ring methylenes; H-4.6 ax downfield),⁴⁴ and 9.79 ppm (0.91H, narrow m., $w_{h/2} = 3$ Hz; -CHO). Upon standing, 19d trimerizes, m.p. 65-70°, δ (CCL/CH₂Cl₂) 4.82 ppm (0.92H vs 9H SiMe₃, t with virtual coupling; trioxane methine). Desilvlation of 51 mg of 22d (0.15 mmole) in 5 ml THF containing 0.18 mmole TBAF resulting in an immediate ppt and formation of 2-(5',5'dimethoxypentyl)-1,3-dithiane (35 mg, 85% yield)-& (CH2Cl2) 3.24 (5.6H, s; OMe), 3.97 (1.00H, t, ~7 Hz; dithiane-H-2), and 4.29 ppm (1.0H, t, ~5 Hz; -CH[OMe]₂)-identical in all respects to material prepared from 1,3-dithian-2-yllithium and bromide 20d. Acetal hydrolysis (HCI-H2O/THF) afforded the dithianealdehyde (17d): δ (CCl₄) 2.84 (4H, m; H-4,6), 3.99 (1H, ~t; H-2), and 9.80 ppm (1H, ~t, CHO).

Aldehyde 19d (154 mg in 1 ml C₆H₆, 0.56 mmole) was added to 16 ml THF containing 0.62 mmole TBAF. After 10 min at room temp., partitioning between water and CH₂Cl₂ afforded 121 mg (~100%) of crude 18d as a yellow oil. Careful chromatography on 15g neutral silica (1-10% EtOAc/hexanes) afforded 66 mg (58% yield) of 18d: EI-MS 204.2 (19, M⁺), 187.2 (100, M-OH), 119 amu (3%, C₄H₇S₂); δ 1.2-3.3 (15.6H integral), 3.99 ppm (1.00H, m, $w_{h/2} = 9$ Hz; CHOH). Silvlation (BSTFA) afforded a single GC homogeneous material (24).

Aldehyde 19d (50 mg/3 ml THF) was treated with 0.1 equiv of TBAF^t for 10 min at -10°. An extractive work-up and chromatographic filtration afforded 36 mg (ca. 70% yield) of a mixture of 18d and its silyl ether (24)-identity confirmed by tlc and NMR comparison with previous specimens.

Synthesis and TBAF induced cyclizations of silyldithianes 19c and 25c. Dithiane 10 (3.364 g, 17.5 mmole) in 70 ml THF was converted to its lithio derivative (1.05 equiv nBuLi, 5 hr at 0°) and to the resulting soln, cooled to -78° , was added 4.18 g (18.6 mmole) 4-trimethylsilyloxybutyl bromide;40 after 2 hr of gradual warming to 0°, partitioning between water and hexane and column chromatography (20% ether in hexane/SiO₂) afforded 4.07 g (88%) of 23. $R_{f}=0.11$ (CH₂Cl₂/SiO₂); δ 0.15 (=9.0H, s, SiMe₃), 3.62 (1.95H, \sim t; CH₂OH). 3.00 (1.90H, dt, J_d \sim 4.5, J_t \sim 12 Hz; H-4,6-ax⁴⁴), 1.8-2.65 (\sim 6H, m), and 1.3-1.8 ppm (\sim 5H, m). A 1.014-g sample of 23 in 50 ml CH₂Cl₂ was treated with 1.262 g PCC⁴¹ (1.46 mmole/mmole alcohol) for 3.5 hr, the resulting mixture diluted with 150 ml Et₂O, filtered and concentrated, was eluted through a 1×10 cm column of SiO₂ (10% Et₂O/CCl₄) affording 615 mg (62%) of 19c: $R_f = 0.51$ (CH₂Cl₂/SiO₂)—suitable for cyclization or Emmons' condensation. Direct cyclization (1.12 equiv TBAF, 10 min) afforded a 76% yield of $18c - R_f = 0.26$ CH₂Cl₂/SiO₂) which was 95⁺% pure by GC: δ (CCL) 1.4 (OH), and 4.14 ppm (1H, $w_{h/2} = 7$ Hz; CHOH).

The Emmon's condensation of 19c (160 mg, 0.61 mmole) employed 1.34 mmole NaH and 1.86 mmole CH₃COCH₂PO(OMe)₂ in precisely the manner described for prostaglandin side-chain synthesis.⁴² After 22 hr, the neutralized mixture afforded 140 mg (76%) of 25c upon column chromatography: $R_f = 0.22$ (CH₂Cl₂/SiO₂); ν 1680, 1630 cm⁻¹ (C=C-C=O δ (CCL₄) 2.13 (3H, s, -COCH₃), 2.96 (2H, dt; H-4,6-ax), 5.99 (1H, d, 16.0 Hz; enone α-H), and 6.73 ppm (1H, dt, 16.0, 6.4 Hz; β -H).

Enone 25c (120 mg, 0.41 mmole) in 25 ml THF was treated with 2.2 ml of 0.29 M TBAF/THF (0.64 mmole) to produce a deep burgundy colored soln. After 1 hr at 22°, partitioning between hexane and water afforded 81 mg of crude product, which displayed no olefinic, Me₃Si, or dithianyl-H-2 NMR resonances. Chromatography on SiO₂ (5% EtOAc/hexane) afforded 60 mg (64%) of 27c: $R_f = 0.28$ (CH₂Cl₂/SiO₂); ν 1717 cm⁻¹; δ (CCl₄) 2.07

(3H, s, -COCH₃), and 2.83 ppm (dithiane-4,6-H pattern, no Δδaxequat.).

2-Vinyl-1,3-dithian-2-yllithium 30a and its reactions with electrophiles. A flamed 25 ml flask was charged with 34 (534 mg, 3.0 mmole of 82% pure material) and THF (2 ml), cooled to -70° , and treated with a soln of lithium diisopropylamide (10 mmole) in 10 ml THF. After 4 hr, the reaction was guenched by addition of trimethylsilyl chloride (20 mmole, 2.54 ml), stirred at -70°, allowed to warm to RT overnight, then worked up with water and CH₂Cl₂. The yellow oil was chromatographed on MN silica gel (2% EtOAc/hexane) to obtain 572 mg (87%) of 32a: MS 220.0560 $(7.7, C_9H_{18}^{32}S^{34}SSi - 1.6), 218,0604 (59, C_9H_{18}S_2Si - 1.4), 145,0152$ (77, C6H9S2 + 0.6), and 73.0458 amu (100%, C1H9Si - 1.6 mmass); δ (CDCl₃) 0.18 (9H, s; SiMe₃), 2.00 (2H, m; H-5), 2.40 (2H, m; H-4,6 equatorial), 2.96 (2H, m; H - 4.6 ax),⁴⁴ 5.37 (2H, BC of vinyl ABC $2J_{BC} = 2.5 \text{ Hz}$, and 6.02 ppm (1H, dd, $3J_{cir} = 9.0$; $3J_{trans} = 17.5$ Hz).

Alternatively solns of 30a could be generated from: 34 by an equimolar amount of nBuLi-TMEDA complex; 12 hr at -20° , then 1 hr at $+22^\circ$; or from 31a⁴³ with 1.05 equiv BuLi at -20° for 1 hr. Stannylation (2.7 equiv Me₃SnCl, 10 hr -60 to -20°) afforded 35 (which was obtained in ca 80% purity, 60% yield) after a quick chromatographic filtration [neutral Al₂O₃ (IV), 2% EtOAc/hexane]: δ (CDCl₃) 0.18 (9H, s; SnMe₃), 1.98 (2H, d, 9 Hz; CH₂SnMe₃), 1.83-2.16 (2H, m; H-5), 2.2-3.0 (4H, m; H-4,6), and 6.26 ppm (IH, t, 9 Hz; vinyl-H). Quenching of 30a solns with MeI affords only isomer 40b.⁴¹ together with minor amounts of 31a and 34. Quenching 30a with 2 equiv of piperonal afforded a ca 9:1 mixture of addition products. The major product was isolated for characterization, (39): 8 (CDCl₃) 1.60-2.36 (4H, complex m; dithiane-H-5 + allyl-CH₂), 2.36-3.03 (4H, m; H-4,6), 4.63 (1H, t, 7 Hz; CHOH), 5.95 (1H, t, 7 Hz; vinyl-H), 5.95 (2H, s; O₂CH₂), and 6.83 ppm (3H, m; aryl-H).

TBAF⁺ induced addition reactions of allylmetalloids (e.g., 32a, 35). The allyl metalloid (1 mmole), piperonal (1 mmole) and THF (4 ml) were mixed in a flamed 10 ml flask under argon. The solns were treated at - 20° with TBAF[‡] (1 ml of 1 M soln in THF). GC analyses indicated complete reaction within 15 min. Standard work-up afforded yellow-brown oils. Tlc (silica, 25% EtOAc/hexane) showed two new products, $R_f = 0.32$ and 0.26, with residual piperonal at $R_f = 0.42$. NMR spectra of the crude products from 32a and 35 showed comparable mixtures. TLC comparison using authentic γ -adduct (39) indicated that the minor product from 32a and 35 corresponded to 39.

For 32a the crude oil (435 mg) was chromatographed twice on a Harrison Research chromatotron (25% EtOAc/hexane) to afford the less polar product (45 mg), and the more polar porduct (10 mg). These were identified respectively as the α -regiochemical adduct and the γ -adduct. The NMR characteristics of the α -adduct (40c) isolated from the reaction of 32a, are— δ (CDCh) ~1.9 (2H, m; H-5), 2.54-3.07 (4H, m; H-4,6), 4.80 (1H, s, $w_{h/2} = 3$ Hz; CHOH), 5.17-5.83 (3H, closed coupled ABC due to -CH=CH₂), 5.96 (2H, s; O_2 CH₂), 6.9 ppm (3H; aryl-H). The γ adduct (39) displayed the NMR reported above.

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an extrapolation based on the measured value below:

$$\frac{\left< \sum_{s}^{s} \right>_{R}^{H}}{pK_{a}(K^{+}, DMSO)} R = \frac{C_{6}H_{5}}{30.7} \frac{pC_{6}H_{5}C_{6}H_{4}}{29.1} - \frac{-CHz}{27.4} - \frac{CO_{2}Me}{20.9} \frac{CN}{19.1}$$

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- ⁴³Vinyldithianes **31a** and **40b** have not been mentioned in the lit, but homologs have been reported and the α/γ regiochemistry of attack has been discussed.^{29,35} They appear with full characterization in the Ph.D. thesis of A. D. Denniston.²⁸ The spectrum of **40b** is essentially identical to that of **40a** except for the C-2-Me singlet at 1.48 ppm.
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