# A HIGHLY STEREOSELECTIVE SYNTHESIS OF Z-1,2-DIALKYLVINYLSILANES
## FROM ACYLSILANE/YLIDE CHEMISTRY

John A. Soderquist* and Charles L. Anderson[1]
Department of Chemistry, University of Puerto Rico
Rio Piedras, Puerto Rico 00931

**Abstract:** *The reaction, in the presence of soluble lithium salts, of non-stabilized ylides at low temperature with aliphatic derivatives of acylsilanes gives moderate to good (37-82%) yields of Z-1,2-disubstituted vinylsilanes in excellent ( >96% ) isomeric purities for normal alkyl derivatives. Implications of these results on the mechanistic aspects of the Wittig olefination are discussed.*

Since its discovery over thirty years ago, the Wittig olefination[2] has engendered continuous synthetic and mechanistic interest.[3] Non-stabilized ylides react with aliphatic aldehydes to give mainly *cis* alkenes, with this selectivity being enhanced by "salt-free" or "lithium ion-sequestering" conditions as well as with increasing bulk on the aldehyde or phosphorus portion of the combining partners.[3e,n] Recently, it has been demonstrated that acylsilanes can function as sterically-modified aldehydes in certain reactions.[4] It occurred to us that the stereo-chemical consequence of substituting an acylsilane for an aldehyde in this process should be to give Z-alkenylsilanes selectively. In such products, the alkyl groups would have the opposite (*trans*) stereochemical relationship, as that which would be obtained from the corresponding aldehyde. Moreover, these compounds would also contain the additional synthetic versatility of the vinylsilane functionality as compared to normal alkene products.[5]
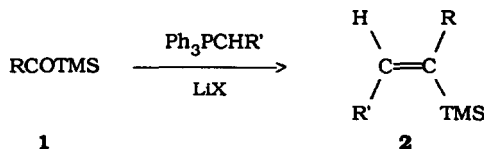


Early studies by Brook[6] clearly established that aliphatic acylsilanes underwent the normal olefination with methylenetriphenylphosphorane, but with this ylide the stereochemistry of the process could not be determined. Thus, we chose to examine representative ylide/aliphatic acylsilane combinations, first with respect to yield optimization (Table 1) and second, to determine the scope and stereoselectivity of the process (Table 2). This data reveals that the best conditions for the preparation of **2** are obtained when **1** is added to the ylide at low temperature in the presence of soluble lithium salts. As expected, no Brook rearrangement products were observed for these aliphatic acylsilanes. To ascertain the product configurations, **2** was photoisomerized to a mixture employing Zweifel's procedure which enabled us to quantitatively analyze the product composition by capillary GC.[7]

Corroborative NMR data reveals the following generalizations: (1) $^1$H NMR: The silicon methyls absorb at slightly higher field for the E vs the Z isomer (eg. **2a**: 0.06 vs 0.10 ). (2) $^{29}$Si NMR: The Z isomer absorbs at higher field than the corresponding E isomer (eg. **2a**: -7.8 vs -4.9 ) with the exception of **2e** (R' = OMe) where the opposite is true (ie. **2e**: -4.8 vs -6.7 ). (3) $^{13}$C NMR: The allylic carbon atoms in the the E isomer are consistently found at higher field than the corresponding carbon atoms in the Z isomer (eg. **2a**: 30.6; 29.6 vs 34.2; 38.3 for C-3,6).[8]

Formation of the enolate of the acylsilane was found to be a major competing process. While the monodeuteration of the enolate was consistently incomplete (*cf.* Table 2),[9] the silylation process was more conclusive in that no unreacted acylsilane was found and **2a** and **3** were formed as the only significant volatile products. Similarly, under "salt-free" conditions (*cf.* Table 1. Entry 9), silylation gives **3** exclusively.
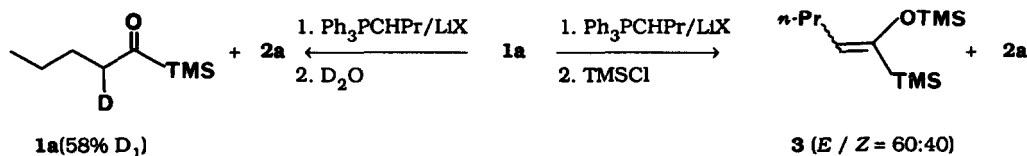


**1a**(58% $D_1$)    **3** (E / Z = 60:40)

TABLE 1. QUANTITATIVE DATA FOR THE REACTION OF 1 WITH $Ph_3PCH(n-Pr)$.[a]

| Entry | R | Base[b] | Solvent System | Temperature | 1 (recovered) | 2 | Total |
|-------|------|---------|----------------|-------------|---------------|---------|-------|
| 1 | n-Bu | n-BuLi | THF | -78 | 33 | 47 | 80 |
| 2 | n-Bu | n-BuLi | THF | -110 | 31 | 56 | 87 |
| 3 | n-Bu | n-BuLi | EE | -110 | 44 | 48 | 92 |
| 4 | n-Bu | n-BuLi | THF/LiI[c] | -110 | 52(42) | 39(36) | 91 |
| 5 | n-Bu | n-BuLi | THF/TMEDA[d] | -110 | 68 | 19 | 87 |
| 6 | n-Bu | n-BuLi | THF/$BF_3$-$Et_2O$[e] | -78 | 74 | 21 | 95 |
| 7 | n-Bu | KH | THF | -78 | 103 | 0 | 103 |
| 8 | n-Bu | KH | PhMe | -78 | 98 | 0 | 98 |
| 9 | n-Bu | n-BuLi | PhMe | -78 | 100 | 0 | 100 |
| 10 | Me | n-BuLi | THF | 0 | 32 | 41 | 73 |
| 11 | Me | n-BuLi | THF | -78 | 6 | 92 | 98 |
| 12 | Me | n-BuLi | THF | -110 | 10 | 88 | 98 |
| 13 | Me | LDA | THF | -78 | 44 | 59 | 103 |
| 14 | Me | LDA | THF/TMEDA[d] | -110 | 22 | 39 | 61 |
| 15 | Me | n-BuLi | THF/TMEDA[d] | -78 | 22 | 61 | 83 |
| 16 | Me | n-BuLi | THF/TMEDA[d] | -110 | 14 | 66 | 80 |

a. Yields were determined by GC analysis of the mixtures with added alkane internal standards and are ± 3%. For R = Me (ie. entries 10-16) the combination of the greater solubility of 1 in the aqueous portion of the quenched reaction mixtures and the comparable retention times to that of solvents introduces more uncertainty in the numerical value of recovered 1 than for the pentanoyl case. b. Base used for the preparation of the ylide. c. LiI (2 eq) was added to the ylide at 0° prior to cooling to -110° and, subsequently, the addition of 1. The yields in parentheses were obtained when 1 eq of LiI was added to 1, and the admixture added to the ylide at -110°. d. 2 eq of $N,N,N',N'$-tetramethylethylenediamine were added to the ylide at 0° prior to cooling to the cited reaction temperature and the addition of 1. e. 15 mol % of $BF_3$ etherate was added to the ylide prior to the addition of 1.

TABLE 2. Z-VINYLSILANES (2) FROM ACYLSILANE/YLIDE COMBINATIONS.

| Entry | R | R' | YIELD[a] OF 2 | Z:E[b] | bp(torr) |
|-------|------|------|---------------|--------|-----------|
| 1 | n-Bu | n-Pr | a 41(55) | 98:2 | 58-9(1.5) |
| 2 | Me | n-Pr | b 82(92) | 96:4 | 89(68) |
| 3 | t-Pr | Me | c 37(49) | 98:2 | 145(760) |
| 4 | $Cl(CH_2)_4$ | n-Pr | d 40(41) | 98:2 | 68-70(0.3) |
| 5 | Me | OMe[c] | e 50(88) | 78:22 | 119-130(760) |
| 6 | t-Bu | n-Pr | f 0[d] | | |
| 7 | t-Pr | n-Pr | g 0 | | |
| 8 | Me | t-Pr | h trace[e] | | |
| 9 | n-Bu | t-Pr | i 0 | | |

a. Isolated (GC). All products exhibited both analytical and spectroscopic data which were wholly consistent with the assigned structures. Several of the reaction mixtures were quenched with $D_2O$ and the starting acylsilane was subjected to GC/MS analysis. After correction for the normal M+1 ions in 1, the extent of monodeuteration was determined in each case: Entry 1, 58%; 3, 56%; 8, 33%; 9, 49%. b. For 2a,b,d the E isomer precedes the Z isomer in the capillary GC analysis with a 30m x 0.25 mm 20% SE-30 column. However, 2c and 2e show the opposite elution ordering. c. t-BuLi was used to generate the ylide in this case whereas n-BuLi was used for all other entries. d. No reaction with the ylide was observed at room temperature. With heating, the acylsilane decomposed without detectable formation of 2f. e. A trace amount of 2h was indicated by GC/MS.

We examined the influence of 1 eq of added anhydrous LiI on the $^{13}C$ NMR spectrum of 1a alone in $C_6D_6$ with the finding that it dissolves completely and shifts the carbonyl carbon ca. 10 ppm downfield to 254 ppm while having little influence on the chemical shift of the α carbon. Thus, the presence of lithium salts is apparently necessary to activate the carbonyl moiety of the acylsilane toward nucleophilic attack by the ylide.[10] However, with more hindered acylsilanes such as isobutyryl- or pivaloyl- trimethylsilane, no significant amount of vinylsilane product (2f or 2g) could be observed with butylidenetriphenylphosphorane. Starting material was recovered in essentially quantitative yields with partial deuteration observed in the former case and in the latter, heating led to ketone decomposition giving a mixture of many products with no detectable amount of 2 being formed by GC/MS analysis. Only the parent methylene ylide was found to undergo olefination with this pivaloyl system (ie. 4h @ rt). By contrast, the ethylidene ylide did give alkenylsilane product, 2c, in moderate yield, with the isobutyrylsilane. Thus, the reaction is remarkably sensitive to the substitution pattern in that an isopropyl group on the acylsilane and a methyl group on the ylide gives the vinylsilane product whereas the opposite arrangement does not. The $Z/E$ ratios reflect the fact that the smaller group combinations (ie. OMe/Me) give significantly lower $Z$ selectivity than do n-Pr/Me or t-Pr/Me (cf. Table 2).[11]

The remarkable Z-selectivity of this process under "soluble salt" conditions is unprecedented in the synthesis

of trisubstituted alkenes.[3,12] The low temperature (*ie.* -90°) ^{31}P NMR (36.4 MHz) demonstrated that **2a** was formed from an oxaphosphetane intermediate which is seen at δ -65.7 ppm[3e] and which is found to smoothly decompose at *ca* -50° to give **2a** and Ph₃PO·LiX (δ 28 ppm). Moreover, the irreversibility of the process was indicated by the complete absence of reaction with added benzaldehyde after the formation of this intermediate from **1a** and the butylidene ylide (δ +12 ppm) (4h at -95°).[13] That significant quantities of betaine-lithium halide complexes are not formed in such processes was demonstrated with the addition of an excess of TMSCl to the mixture used to prepare **2b** (*cf.* Table 1, Entry 12) with no detectable affect on the vinylsilane formation.[14]

A number of models have been advanced to explain the Z-selectivity in the Wittig olefination.[3,15] The recent discovery by Maryanoff[3n] that lithium ion catalysis only modestly diminishes the Z-selectivity for irreversible aldehyde/ylide reactions suggests that the factors which govern the kinetic selectivity of both this and the "salt-free" reaction could be quite similar. Fortunately, our systems not only form oxaphosphetanes (*cf.* **4**) irreversibly, but also, these intermediates smoothly decompose to give Z-vinylsilane products of high stereochemical purities. Under "salt-free" conditions, the ylides function only as bases. Thus, these sensitive systems provide a complementary window of information to that which is currently available for the Wittig process. As we view it, the major problem in the mechanistic interpretation of the Wittig process is how to deal with the fact that E oxaphosphetanes are apparently more stable than their Z counterparts and yet, they are formed more slowly. No structural evidence is available for the isomeric oxaphosphetanes which are observed by ^{31}P NMR. However, Ramirez's isolable system[16] does provide a basis for the structural features which we have used for **4**. Our data suggests that, if involved, open betaine-LiX complexes[17] can only be transient intermediates, possibly in equilibrium with the starting materials, but not with the oxaphosphetane, **4**. We propose that, at low temperatures, the lithium ion activated acylsilane[18] reacts irreversibly and, necessarily, exothermically with ylides to form **4**, with the illustrated nonplanar ring geometry.[16] This bent geometry suggests a favored *distorted anticlinal* approach to this intermediate with mutual repulsions between the largest groups (*viz.* TMS and PPh₃) being responsible for this distortion.[19] Moreover, the greater the difference in size between the TMS *vs* R ( or, R *vs* H in the case of aldehydes ), the more deflected the large phosphonio group will be. These intermediates decompose at higher temperatures, perhaps through pseudorotamers[3h] (*ie.* **4'**), to produce **2** and Ph₃PO·LiX. Focusing on the R' group in such an intermediate, it must interact either with the TMS group *and* an equatorial phenyl (**4Z**) *or* with the R group *and* an apical phenyl group (**4E**). Thus, in our crowded system, we note that only small R' groups can be accommodated in **4**, and our experimental data supports this conclusion. Moreover, as R becomes larger, the oxaphosphetane would be expected to be flatter. Even less bulk in R' can be tolerated due to unavoidable steric replusions from either the TMS or R groups. Vedejs[15] has recently shown that one small group on phosphorus is sufficient to give a *trans*-selective olefination. Thus, it would follow directly from our model for **4** that replacement of the apical phenyl group with a smaller alkyl or alkoxy group would result in a lowering of the severe 90° interaction between the pseudoaxial R' group and the apical phosphorus ligand, resulting, in this case, in **4E** with its pseudoequatorial R' group, being more stable than **4Z**, consistent with the structural[16] and experimental[15] data. For the triphenyl substitution, our arguments clearly imply that **4Z** is both formed faster and is more stable than **4E**. The opposite relative stabilities would be expected for the pseudorotamers, **4'E** and **4'Z**, where R' interacts with phosphorus ligands at 90° in both cases but less with the TMS in the former case. This *crossover in the relative stabilities* and to the extent that this is felt in the transition state energies leading from the observed oxaphosphetanes to alkene products could be the reason that *trans* oxaphosphetanes decompose slower than their *cis* counterparts. In this way, both kinetic aspects of the Wittig process are modeled. Further studies are underway to evaluate the applicability of these arguments to other systems.
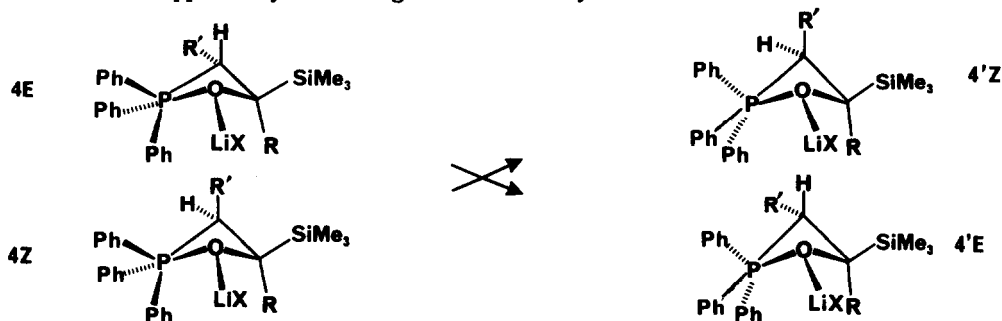
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13. While isomerization studies indicate that simple *trans*-1-silylalkenes are more stable than their *cis* counterparts, the relative stabilities of the 1,2-substituted vinylsilanes are less clear.[7] Also, our MM2 calculations suggest that while the *trans* compounds are more stable in the former case, in the latter case, the Z isomer is either equal in energy to (*eg.* 2b) or more stable than (*eg.* 2a,c) the E isomer. It is thus, unlikely, that our product distributions represent equilibrium mixtures.

14. While HCl or HBr are normally employed to convert either betaine-lithium halide complexes or oxaphosphetanes to β-hydroxyphosphonium salts, TMSCl would be expected to trap the former (*cf.* ref. 5a-e). The present study demonstrates that the latter does not react with this reagent to any significant extent.

15. *Note added in proof.* During the reviewing process, Professor Vedejs was kind enough to send us a preprint of his manuscript in which he considers the role played by the phosphorus ligands on the selectivity of oxaphosphetane formation. His arguments are based upon an sp³ phosphorus in the transition state, demonstrating the influence played by a smaller ligand in strategically designed ylides. We thank Professor Vedejs for helpful discussions regarding this work. (*cf.* Vedejs, E.; Fleck, T.; Hara, S. *J. Org. Chem.* **1987**, *52*, 4637 and Vedejs, E.; Marth, C. F. *J. Am. Chem. Soc.*, in press.)

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17. Such species could well account for the lithium ion promoted Brook rearrangement of aroylsilanes[6] and its homo-Brook counterpart (*cf.* ref. 5k). However, both the sensitivity of the substitution pattern and lack of effect with TMSCl after the formation of 4, support our interpretation. For the consequence of this on the stereochemistry of the overall reaction, see Curtin, D. Y. *Rec. Chem. Prog.* **1954**, *15*, 111.

18. The presence of coordinated lithium ion would be expected to serve to not only to increase the electrophilicity of the carbonyl carbon atom through an increase of the component of the LUMO at that carbon allowing the T.S. to be reached earlier,[3p] but also to increase the bond angles of the groups attached to that carbonyl at the expense of the angles between the carbonyl and those groups,[10] thus lowering the Z selectivity in standard systems compared to "salt-free" conditions. Recent studies by Maryanoff[3n] have indicated that lithium ions can alter the initial *erythro/threo* selectivity of the adducts formed from aliphatic aldehyde/ylide combinations but the reactions remain irreversible as under "salt-free" conditions.

19. The approach[3e,15] may not be strictly perpendicular (*cf.* Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 2819.) The similar bond lengths for P-C and Si-C (*cf.* Weast, R. C.; Astle, M. J. (Eds.) "CRC Handbook of Chemistry and Physics" 62nd Ed., CRC Press, Inc.: Boca Raton, Florida, 1981) would be expected to result in large steric repulsions between these groups.